IDENTIFYING DRUGS FOR AND DIAGNOSIS OF BENIGN PROSTATIC HYPERPLASIA USING GENE EXPRESSION PROFILES

INVENTORS: WILLIAM E. MUNGER, PRAKASH KULKARNI, ROBERT H. GETZENBERG, IWAO WAGA AND JUN YAMAMOTO

RELATED APPLICATIONS

[0001] This application claims priority of U.S. Provisional Application No. 60/223,323, filed August 7, 2000, which is herein incorporated by reference in its entirety.

BACKGROUND OF THE INVENTION

[0002] Benign Prostatic Hyperplasia (BPH) is the most common benign tumor in men aged >60 years. It is estimated that one in four men living to the age of 80 will require treatment for this disease. BPH is usually noted clinically after the age of 50, the incidence increasing with age, but as many as two thirds of men between the ages of 40 and 49 demonstrate histological evidence of the disease.

[0003] The anatomic location of the prostate at the bladder neck enveloping the urethra plays an important role in the pathology of BPH, including bladder outlet obstruction. Two prostate components are thought to play a role in bladder outlet obstruction. The first is the relative increased prostate tissue mass. The second component is the prostatic smooth muscle tone.

[0004] The causative factors of BPH in man have been intensively studied. See Ziada *et al.*, *Urology*, 53: 1-6, 1999. In general, the two most important factors appear to be aging and the presence of functional testes. Although these factors appear to be key to the development of BPH, both appear to be nonspecific.

[0005] Little is known about the molecular changes in prostate cells associated with the development and progression of BPH. It has been demonstrated that the expression levels of a number of individual genes are changed compared to normal prostate cells. These changes in gene expression include decreased expression of Wilm's tumor gene (WT-1) and increased expression of insulin growth factor II (IGF-II) (Dong *et al.*, *J. Clin. Endocrin. Metab.*, 82(7): 2198-220).

[0006] While the changes in the expression levels of a number of individual genes have been identified, the investigation of the global changes in gene expression has not been reported.

[0007] Accordingly, there exists a need for the investigation of the changes in global gene expression levels as well as the need for the identification of new molecular markers associated with the development and progression of BPH. Furthermore, if intervention is expected to be successful in halting or slowing down BPH, means of accurately assessing the early manifestations of BPH need to be established. One way to accurately assess the early manifestations of BPH is to identify markers which are uniquely associated with disease progression. Likewise, the development of therapeutics to prevent or stop the progression of BPH relies on the identification of genes responsible for BPH growth and function.

SUMMARY OF THE INVENTION

[0008] The present invention is based on the elucidation of the global changes in gene expression in BPH tissue isolated from patients exhibiting different clinical states of prostate hyperplasia as compared to normal prostate tissue as well as the identification of individual genes that are differentially expressed in BPH tissue.

[0009] The invention is also based on the discovery of a means of effectively selecting disease-linked drug targets from gene expression results. The invention includes methods of classifying genes whose expression levels are changed in diseased tissues, during disease induction or during disease progression into specific groups. By using this method it is possible to classify genes whose expression are regulated by the same mechanism into the same group, and it is possible to identify representative marker genes by selecting typical genes from each cluster.

[0010] The invention includes methods of screening for or identifying an agent that modulates the onset or progression of BPH, comprising: preparing a first gene expression profile of BPH cells; exposing the cells to the agent; preparing a second gene expression profile of the agent exposed cells; and comparing the first and second gene expression profiles. In a preferred embodiment of these methods, the gene expression profile comprises the expression levels of one or more or preferably two or more genes in Tables 1-5. In another preferred embodiment of these methods, the cell is a prostate cell from a BPH patient, a cell line in Table 6, or a derivative thereof.

[0011] The invention also includes methods of monitoring a treatment of a patient with BPH, comprising administering a pharmaceutical composition to the patient; preparing a gene expression profile from a prostate cell or tissue sample from the patient; and comparing the patient gene expression profile to a gene expression profile from a normal prostate cell population, a BPH tissue or BPH cells without treatment with the pharmaceutical composition. In

preferred embodiments of these methods, the gene expression profile comprises the expression levels of one or more or, preferably two or more genes in Tables 1-5.

[0012] The invention also includes methods of diagnosing benign prostatic hyperplasia (BPH) in a subject comprising the step of detecting the level of expression in a tissue or cell sample from the subject of two or more genes from Tables 1-5 (preferably Tables 3-5, and more preferably Table 5); wherein differential expression of the genes is indicative of BPH progression.

[0013] The invention further includes methods of detecting the onset or progression of benign prostatic hyperplasia (BPH) in a patient comprising the step of detecting the level of expression in a tissue or cell sample of two or more genes from Tables 1-5 (preferably Tables 3-5, and more preferably Table 5); wherein differential expression of the genes is indicative of BPH progression.

[0014] The invention also includes methods of differentiating benign prostatic hyperplasia (BPH) from prostate cancer in a patient comprising the step of detecting the level of expression in a tissue or cell sample of two or more genes from Tables 1-5 (preferably Tables 3-5, and more preferably Table 5); wherein differential expression of the genes is indicative of BPH rather than prostate cancer.

[0015] The invention also includes methods of selecting or identifying cells that can be used for drug screening.

[0016] All of these methods may include the step of detecting the expression levels of at least about 2, 3, 4, 5, 6, 7, 8, 9, 10 or more genes in any of Tables 1-5, or preferably Table 5. In a preferred embodiment, expression of all of the genes or nearly all of the genes in Tables 1-5, or preferably Table 5, may be detected.

[0017] The invention further includes sets of at least two or more probes, wherein each of the probes comprises a sequence that specifically hybridizes to a gene in Tables 1-5 as well as solid supports comprising at least two or more of the probes.

[0018] The invention also includes computer systems comprising or linked to a database containing information identifying the expression level in BPH tissue or cells of a set of genes comprising at least two genes in Tables 1-5, preferably from Table 5; and a user interface to view the information. The database may further comprise sequence information for the genes as well as information identifying the expression level for the set of genes in normal prostate tissue or cells, and prostate cancer tissue. The database may further contain or be linked to descriptive

information from an external database, which information correlates said genes to records in the external database.

[0019] The invention further includes methods of using the disclosed computer systems to present information identifying the expression level in a tissue or cell of a set of genes comprising at least one of the genes in Tables 1-5, preferably Table 5, comprising comparing the expression level of at least one gene in Tables 1-5, preferably Table 5, in the tissue or cell to the level of expression of the gene in the database.

[0020] Lastly, the invention includes kits comprising probes or solid supports of the invention. In some embodiments, the kits also contain written materials or software concerning gene expression information for the genes of the invention, preferably in electronic format.

BRIEF DESCRIPTION OF THE DRAWINGS

[0021] Figure 1. Figure 1 shows the expression of cellular retinol binding protein RNA in various tissues.

[0022] Figure 2. Figure 2 shows the expression of cellular retinol binding protein RNA in various prostate tissues samples. In all of the figures, "Normal", "-Sym", "Cancer" and "+Sym" refer to normal prostate, BPH without symptoms, prostate cancer, and BPH with symptoms, respectively.

[0023] Figure 3. Figure 3 shows the expression of S100 calcium binding protein RNA in various tissues.

[0024] Figure 4. Figure 4 shows the expression of S100 calcium binding protein RNA in various prostate tissue samples.

[0025] Figure 5. Figure 5 shows the expression of PSMA RNA in various tissues.

[0026] Figure 6. Figure 6 shows the expression of PSMA RNA in various prostate tissue samples.

DETAILED DESCRIPTION

[0027] Many biological functions are accomplished by altering the expression of various genes through transcriptional (*e.g.* through control of initiation, provision of RNA precursors, RNA processing, etc.) and/or translational control. For example, fundamental biological processes such as cell cycle, cell differentiation and cell death, are often characterized by the variations in the expression levels of groups of genes.

[0028] Changes in gene expression also are associated with pathogenesis. For example, the lack of sufficient expression of functional tumor suppressor genes and/or the over expression of oncogene/protooncogenes could lead to tumorgenesis or hyperplastic growth of cells (Marshall, Cell, 64: 313-326 (1991); Weinberg, Science, 254:1138-1146 (1991)). Thus, changes in the expression levels of particular genes (*e.g.* oncogenes or tumor suppressors) serve as signposts for the presence and progression of various diseases.

[0029] Monitoring changes in gene expression may also provide certain advantages during drug screening development. Often drugs are screened for the ability to interact with a major target without regard to other effects the drugs have on cells. Often such other effects cause toxicity in the whole animal, which prevent the development and use of the potential drug.

[0030] The present inventors have examined tissue from normal prostate, BPH and BPH prostate tissue immediately adjacent to malignant prostate tissue to identify the global changes in gene expression in BPH. These global changes in gene expression, also referred to as expression profiles, provide useful markers for diagnostic uses as well as markers that can be used to monitor disease states, disease progression, toxicity, drug efficacy and drug metabolism.

Assay Formats

[0031] The genes identified as being differentially expressed in BPH tissue or BPH cells (Tables 1-5) may be used in a variety of nucleic acid detection assays to detect or quantititate the expression level of a gene or multiple genes in a given sample. For example, traditional Northern blotting, nuclease protection, RT- PCR and differential display methods may be used for detecting gene expression levels. Those methods are useful for some embodiments of the invention. However, methods and assays of the invention are most efficiently designed with hybridization-based methods for detecting the expression of a large number of genes.

[0032] Any hybridization assay format may be used, including solution-based and solid support-based assay formats. Solid supports containing oligonucleotide probes for differentially expressed genes of the invention can be filters, polyvinyl chloride dishes, silicon or glass based beads or chips, etc. Such supports and hybridization methods are widely available, for example, those disclosed by Beattie (WO 95/11755). Any solid surface to which oligonucleotides can be bound, either directly or indirectly, either covalently or non-covalently, can be used.

[0033] A preferred solid support is a high density array or DNA chip. These contain a particular oligonucleotide probe in a predetermined location on the array. Each predetermined location

may contain more than one molecule of the probe, but each molecule within the predetermined location has an identical sequence. Such predetermined locations are termed features. There may be, for example, from 2, 10, 100, 1000 to 10,000, 100,000 or 400,000 of such features on a single solid support. The solid support, or the area within which the probes are attached may be on the order of about a square centimeter.

[0034] Oligonucleotide probe arrays for expression monitoring can be made and used according to any technique known in the art (see for example, Lockhart *et al.*, Nat. Biotechnol. (1996) 14, 1675-1680; McGall *et al.*, *Proc. Nat. Acad. Sci. USA* (1996) 93, 13555-13460). Such probe arrays may contain at least two or more oligonucleotides that are complementary to or hybridize to two or more of the genes described in Tables 1-5 . For instance, such arrays may contain oligonucleotides that are complementary or hybridize to at least about 2, 3, 4, 5, 6, 7, 8, 9, 10, 20, 30, 50, 70 or more the genes described herein.

[0035] The genes which are assayed according to the present invention are typically in the form of mRNA or reverse transcribed mRNA. The genes may be cloned or not. The genes may be amplified or not. The cloning itself does not appear to bias the representation of genes within a population. However, it may be preferable to use polyA+ RNA as a source, as it can be used with less processing steps.

[0036] The sequences and related information of the genes described herein are available in the public databases. Tables 1-5 provide the Accession numbers and name for each of the sequences. The sequences and related information of the genes listed in the Tables according to their GenBank identifiers are expressly incorporated herein as of the filing date of this application (see: www.ncbi.nlm.nih.gov/).

[0037] Probes based on the sequences of the genes described above may be prepared by any commonly available method. Oligonucleotide probes for interrogating the tissue or cell sample are preferably of sufficient length to specifically hybridize only to appropriate, complementary genes or transcripts. Typically the oligonucleotide probes will be at least 10, 12, 14, 16, 18, 20 or 25 nucleotides in length. In some cases longer probes of at least 30, 40, or 50 nucleotides will be desirable.

[0038] As used herein, oligonucleotide sequences that are complementary to one or more of the genes described in Tables 1-5 refer to oligonucleotides that are capable of hybridizing under stringent conditions to at least part of the nucleotide sequence of said genes. Such hybridizable oligonucleotides will typically exhibit at least about 75% sequence identity at the nucleotide level

to said genes, preferably about 80% or 85% sequence identity or more preferably about 90% or 95% or more sequence identity to said genes.

[0039] "Bind(s) substantially" refers to complementary hybridization between a probe nucleic acid and a target nucleic acid and embraces minor mismatches that can be accommodated by reducing the stringency of the hybridization media to achieve the desired detection of the target polynucleotide sequence.

[0040] The terms "background" or "background signal intensity" refer to hybridization signals resulting from non-specific binding, or other interactions, between the labeled target nucleic acids and components of the oligonucleotide array (*e.g.*, the oligonucleotide probes, control probes, the array substrate, *etc.*). Background signals may also be produced by intrinsic fluorescence of the array components themselves. A single background signal can be calculated for the entire array, or a different background signal may be calculated for each target nucleic acid. In a preferred embodiment, background is calculated as the average hybridization signal intensity for the lowest 5% to 10% of the probes in the array, or, where a different background signal is calculated for each target gene, for the lowest 5% to 10% of the probes for each gene. Of course, one of skill in the art will appreciate that where the probes to a particular gene hybridize well and thus appear to be specifically binding to a target sequence, they should not be used in a background signal calculation. Alternatively, background may be calculated as the average hybridization signal intensity produced by hybridization to probes that are not complementary to any sequence found in the sample (*e.g.* probes directed to nucleic acids of the opposite sense or to genes not found in the sample such as bacterial genes where the sample is mammalian nucleic acids). Background can also be calculated as the average signal intensity produced by regions of the array that lack probes.

[0041] The phrase "hybridizing specifically to" refers to the binding, duplexing, or hybridizing of a molecule substantially to or only to a particular nucleotide sequence or sequences under stringent conditions when that sequence is present in a complex mixture (*e.g.*, total cellular DNA or RNA).

[0042] Assays and methods of the invention may utilize available formats to simultaneously screen at least about 100, preferably about 1000, more preferably about 10,000 and most preferably about 1,000,000 different nucleic acid hybridizations.

[0043] As used herein a "probe" is defined as a nucleic acid molecule, capable of binding to a target nucleic acid of complementary sequence through one or more types of chemical bonds, usually through complementary base pairing, usually through hydrogen bond formation. As used

herein, a probe may include natural (*i.e.*, A, G, U, C, or T) or modified bases (7-deazaguanosine, inosine, *etc.*). In addition, the bases in probes may be joined by a linkage other than a phosphodiester bond, so long as it does not interfere with hybridization. Thus, probes may be peptide nucleic acids in which the constituent bases are joined by peptide bonds rather than phosphodiester linkages.

[0044] The term "stringent conditions" refers to conditions under which a probe will hybridize to its target subsequence, but with only insubstantial hybridization to other sequences or to other sequences such that the difference may be identified. Stringent conditions are sequence-dependent and will be different in different circumstances. Longer sequences hybridize specifically at higher temperatures. Generally, stringent conditions are selected to be about 5oC lower than the thermal melting point (Tm) for the specific sequence at a defined ionic strength and pH.

[0045] Typically, stringent conditions will be those in which the salt concentration is at least about 0.01 to 1.0 M Na ion concentration (or other salts) at pH 7.0 to 8.3 and the temperature is at least about 30°C for short probes (*e.g.*, 10 to 50 nucleotide). Stringent conditions may also be achieved with the addition of destabilizing agents such as formamide.

[0046] The "percentage of sequence identity" or "sequence identity" is determined by comparing two optimally aligned sequences or subsequences over a comparison window or span, wherein the portion of the polynucleotide sequence in the comparison window may optionally comprise additions or deletions (*i.e.*, gaps) as compared to the reference sequence (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical submit (*e.g.* nucleic acid base or amino acid residue) occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the window of comparison and multiplying the result by 100 to yield the percentage of sequence identity. Percentage sequence identity when calculated using the programs GAP or BESTFIT (see below) is calculated using default gap weights.

Probe design

[0047] One of skill in the art will appreciate that an enormous number of array designs are suitable for the practice of this invention. The high density array will typically include a number of probes that specifically hybridize to the sequences of interest. See WO 99/32660 for methods

of producing probes for a given gene or genes. In addition, in a preferred embodiment, the array will include one or more control probes.

[0048] High density array chips of the invention include "test probes." Test probes could be oligonucleotides that range from about 5 to about 500 or 5 to about 45 nucleotides, more preferably from about 10 to about 40 nucleotides and most preferably from about 15 to about 40 nucleotides in length. In other particularly preferred embodiments the probes are 20 or 25 nucleotides in length. In another preferred embodiment, test probes are double or single strand DNA sequences. DNA sequences are isolated or cloned from natural sources or amplified from natural sources using native nucleic acid as templates. These probes have sequences complementary to particular subsequences of the genes whose expression they are designed to detect. Thus, the test probes are capable of specifically hybridizing to the target nucleic acid they are to detect (the genes of Tables 1-5).

[0049] The term "perfect match probe" refers to a probe that has a sequence that is perfectly complementary to a particular target sequence. The probe is typically perfectly complementary to a portion (subsequence) of the target sequence. The perfect match (PM) probe can be a "test probe", a "normalization control" probe, an expression level control probe and the like. A perfect match control or perfect match probe is, however, distinguished from a "mismatch control" or "mismatch probe."

[0050] In addition to test probes that bind the target nucleic acid(s) of interest, the high density array can contain a number of control probes. The control probes fall into three categories referred to herein as 1) normalization controls; 2) expression level controls; and 3) mismatch controls.

[0051] Normalization controls are oligonucleotide or other nucleic acid probes that are complementary to labeled reference oligonucleotides or other nucleic acid sequences that are added to the nucleic acid sample to be screened. The signals obtained from the normalization controls after hybridization provide a control for variations in hybridization conditions, label intensity, "reading" efficiency and other factors that may cause the signal of a perfect hybridization to vary between arrays. In a preferred embodiment, signals (*e.g.*, fluorescence intensity) read from all other probes in the array are divided by the signal (*e.g.*, fluorescence intensity) from the control probes thereby normalizing the measurements.

[0052] Virtually any probe may serve as a normalization control. However, it is recognized that hybridization efficiency varies with base composition and probe length. Preferred normalization probes are selected to reflect the average length of the other probes present in the array, however,

they can be selected to cover a range of lengths. The normalization control(s) can also be selected to reflect the (average) base composition of the other probes in the array, however in a preferred embodiment, only one or a few probes are used and they are selected such that they hybridize well (*i.e.*, no secondary structure) and do not match any target-specific probes.

[0053] Expression level controls are probes that hybridize specifically with constitutively expressed genes in the biological sample. Virtually any constitutively expressed gene provides a suitable target for expression level controls. Typically expression level control probes have sequences complementary to subsequences of constitutively expressed "housekeeping genes" including, but not limited to an actin gene, the transferrin receptor gene, the GAPDH gene, and the like.

[0054] Mismatch controls or mismatch probes may also be provided for the probes to the target genes, for expression level controls or for normalization controls. Mismatch controls are oligonucleotide probes or other nucleic acid probes identical to their corresponding test or control probes except for the presence of one or more mismatched bases. A mismatched base is a base selected so that it is not complementary to the corresponding base in the target sequence to which the probe would otherwise specifically hybridize. One or more mismatches are selected such that under appropriate hybridization conditions (*e.g.*, stringent conditions) the test or control probe would be expected to hybridize with its target sequence, but the mismatch probe would not hybridize (or would hybridize to a significantly lesser extent). Preferred mismatch probes contain a central mismatch. Thus, for example, where a probe is a 20 mer, a corresponding mismatch probe will have the identical sequence except for a single base mismatch (*e.g.*, substituting a G, a C or a T for an A) at any of positions 6 through 14 (the central mismatch).

[0055] Mismatch probes thus provide a control for non-specific binding or cross hybridization to a nucleic acid in the sample other than the target to which the probe is directed. Mismatch probes also indicate whether a hybridization is specific or not. For example, if the target is present the perfect match probes should be consistently brighter than the mismatch probes. In addition, if all central mismatches are present, the mismatch probes can be used to detect a mutation. The difference in intensity between the perfect match and the mismatch probe provides a good measure of the concentration of the hybridized material.

Nucleic Acid Samples

[0056] As is apparent to one of ordinary skill in the art, nucleic acid samples used in the methods and assays of the invention may be prepared by any available method or process. Methods of isolating total mRNA are well known to those of skill in the art. For example, methods of isolation and purification of nucleic acids are described in detail in Chapter 3 *of Laboratory Techniques in Biochemistry and Molecular Biology*: *Hybridization With Nucleic Acid Probes*, Part I Theory and Nucleic Acid Preparation, P. Tijssen, Ed., Elsevier, N.Y. (1993). Such samples include RNA samples, but also include cDNA synthesized from a mRNA sample isolated from a cell or tissue of interest. Such samples also include DNA amplified from the cDNA, and RNA transcribed from the amplified DNA. One of skill in the art would appreciate that it is desirable to inhibit or destroy RNase present in homogenates before homogenates can be used.

[0057] Biological samples may be of any biological tissue or fluid or cells from any organism as well as cells raised in vitro, such as cell lines and tissue culture cells. Biological samples may also include sections of tissues, such as frozen sections or formalin fixed sections taken for histological purposes. Frequently, the sample will be a "clinical sample" which is a sample derived from a patient. Typical clinical samples include, but are not limited to prostate tissue, urine, sputum, blood, blood-cells (*e.g.*, white cells or peripheral blood leukocytes (PBL), tissue or fine needle biopsy samples, peritoneal fluid, and pleural fluid, or cells therefrom.

Forming High Density Arrays.

[0058] Methods of forming high density arrays of oligonucleotides with a minimal number of synthetic steps are known. The oligonucleotide analogue array can be synthesized on a solid substrate by a variety of methods, including, but not limited to, light-directed chemical coupling, and mechanically directed coupling. See Pirrung *et al.*, U.S. Patent No. 5,143, 854.

[0059] In brief, the light-directed combinatorial synthesis of oligonucleotide arrays on a glass surface proceeds using automated phosphoramidite chemistry and chip masking techniques. In one specific implementation, a glass surface is derivatized with a silane reagent containing a functional group, *e.g.*, a hydroxyl or amine group blocked by a photolabile protecting group. Photolysis through a photolithogaphic mask is used selectively to expose functional groups which are then ready to react with incoming 5' photoprotected nucleoside phosphoramidites. The phosphoramidites react only with those sites which are illuminated (and thus exposed by removal of the photolabile blocking group). Thus, the phosphoramidites only add to those areas

selectively exposed from the preceding step. These steps are repeated until the desired array of sequences have been synthesized on the solid surface. Combinatorial synthesis of different oligonucleotide analogues at different locations on the array is determined by the pattern of illumination during synthesis and the order of addition of coupling reagents.

[0060] In addition to the foregoing, additional methods which can be used to generate an array of oligonucleotides on a single substrate are described WO 93/09668. High density nucleic acid arrays can also be fabricated by depositing premade or natural nucleic acids in predetermined positions. Synthesized or natural nucleic acids are deposited on specific locations of a substrate by light directed targeting and oligonucleotide directed targeting. Another embodiment uses a dispenser that moves from region to region to deposit nucleic acids in specific spots.

Hybridization

[0061] Nucleic acid hybridization simply involves contacting a probe and target nucleic acid under conditions where the probe and its complementary target can form stable hybrid duplexes through complementary base pairing. See WO 99/32660. The nucleic acids that do not form hybrid duplexes are then washed away leaving the hybridized nucleic acids to be detected, typically through detection of an attached detectable label. It is generally recognized that nucleic acids are denatured by increasing the temperature or decreasing the salt concentration of the buffer containing the nucleic acids. Under low stringency conditions (*e.g.*, low temperature and/or high salt) hybrid duplexes (*e.g.*, DNA:DNA, RNA:RNA, or RNA:DNA) will form even where the annealed sequences are not perfectly complementary.

[0062] Thus specificity of hybridization is reduced at lower stringency. Conversely, at higher stringency (*e.g.*, higher temperature or lower salt) successful hybridization tolerates fewer mismatches. One of skill in the art will appreciate that hybridization conditions may be selected to provide any degree of stringency. In a preferred embodiment, hybridization is performed at low stringency in this case in 6X SSPE-T at 37°C (0.005% Triton X-100) to ensure hybridization and then subsequent washes are performed at higher stringency (*e.g.*, I X SSPE-T at 37oC) to eliminate mismatched hybrid duplexes. Successive washes may be performed at increasingly higher stringency (*e.g.*, down to as low as 0.25 X SSPET at 37°C to 50°C) until a desired level of hybridization specificity is obtained. Stringency can also be increased by addition of agents such as formamide. Hybridization specificity may be evaluated by comparison of hybridization to the

test probes with hybridization to the various controls that can be present (*e.g.*, expression level control, normalization control, mismatch controls, *etc.*).

[0063] In general, there is a tradeoff between hybridization specificity (stringency) and signal intensity. Thus, in a preferred embodiment, the wash is performed at the highest stringency that produces consistent results and that provides a signal intensity greater than approximately 10% of the background intensity. Thus, in a preferred embodiment, the hybridized array may be washed at successively higher stringency solutions and read between each wash. Analysis of the data sets thus produced will reveal a wash stringency above which the hybridization pattern is not appreciably altered and which provides adequate signal for the particular oligonucleotide probes of interest.

Signal Detection

[0064] The hybridized nucleic acids are typically detected by detecting one or more labels attached to the sample nucleic acids. The labels may be incorporated by any of a number of means well known to those of skill in the art. See WO 99/32660.

Databases

[0065] The present invention includes relational databases containing sequence information, for instance for the genes of Tables 1-5, as well as gene expression information in various prostate tissue samples. Databases may also contain information associated with a given sequence or tissue sample such as descriptive information about the gene associated with the sequence information, metabolic pathway information for the gene or descriptive information concerning the clinical status of the tissue sample, or the patient from which the sample was derived. Such information for the patient may include, but is not limited to sex, age, disease status, general health information, surgical or treatment status, PSA levels, as well as information concerning the patient's clinical symptoms. The database may be designed to include different parts, for instance a sequence database and a gene expression database. Methods for the configuration and construction of such databases are widely available, for instance, see U.S. Patent 5,953,727, which is herein incorporated by reference in its entirety.

[0066] The databases of the invention may be linked to an outside or external database. In a preferred embodiment, as described in Tables 1-5, the external database is GenBank and the associated databases maintained by the National Center for Biotechnology Information (NCBI).

[0067] Any appropriate computer platform may be used to perform the necessary comparisons between sequence information, gene expression information and any other information in the database or provided as an input. For example, a large number of computer workstations are available from a variety of manufacturers, such has those available from Silicon Graphics. Client/server environments, database servers and networks are also widely available and appropriate platforms for the databases of the invention.

[0068] The databases of the invention may be used to produce, among other things, electronic Northerns that allow the user to determine the cell type or tissue in which a given gene is expressed and to allow determination of the abundance or expression level of a given gene in a particular tissue or cell.

[0069] The databases of the invention may also be used to present information identifying the expression level in a tissue or cell of a set of genes comprising at least two of the genes in Tables 1-5, comprising the step of comparing the expression level of at least one gene in Tables 1-5 found or detected in the tissue to the level of expression of the gene in the database. Such methods may be used to predict the hyperplastic state of a given tissue by comparing the level of expression of a gene or genes in Tables 1-5 from a sample to the expression levels found in normal prostate cells, BPH cells or tissue and/or malignant or cancerous prostate tissue. Such methods may also be used in the drug or agent screening assays as described below.

Selection of BPH-Associated Genes

[0070] BPH associated genes may be identified or selected by any available method, including subtractive hybridization protocols, differential display protocols and high-throughput hybridization formats, including oligonucleotide and cDNA microarray technologies.

[0071] Unprocessed or raw expression levels may be normalized, standardized and/or analyzed by any available computational method, including the expression level normalization, analysis and clustering methods herein described. The normalization method as described in Example 4 may be combined with any further analysis method, including any clustering methods available in the art.

Diagnostic Uses for the BPH Markers

[0072] As described above, the genes and gene expression information provided in Tables 1-5 may be used as diagnostic markers for the prediction or identification of the hyperplastic state of a prostate or other tissue. For instance, a prostate tissue or other patient sample may be assayed by any of the methods described above, and the expression levels from a gene or genes from Tables 1-5 may be compared to the expression levels found in normal prostate tissue, BPH tissue or BPH tissue from a patient with metastatic or nonmetastatic prostate cancer. In some instances, patient PBLs may be used as the patient sample. The comparison of expression data, as well as available sequence or other information may be done by researcher or diagnostician or may be done with the aid of a computer and databases as described above.

Use of the BPH Markers for Monitoring Disease Progression

[0073] As described above, the genes and gene expression information provided in Tables 1-5 may also be used as markers for the monitoring of disease progression, such as the development of BPH. For instance, a prostate tissue or other patient sample may be assayed by any of the methods described above, and the expression levels from a gene or genes from Tables 1-5 may be compared to the expression levels found in normal prostate tissue, BPH tissue or BPH tissue from a patient with metastatic or nonmetastatic prostate cancer. The comparison of the expression data, as well as available sequence or other information may be done by researcher or diagnostician or may be done with the aid of a computer and databases as described above.

[0074] The BPH markers of the invention may also be used to track or predict the progress or efficacy of a treatment regime in a patient. For instance, a patient's progress or response to a given drug may be monitored by creating a gene expression profile from a tissue or cell sample after treatment or administration of the drug. The gene expression profile may then be compared to a gene expression profile prepared from normal cells or tissue, for instance, normal prostate tissue. The gene expression profile may also be compared to a gene expression profile prepared from BPH or malignant prostate cells, or from tissue or cells from the same patient before treatment. The gene expression profile may be made from at least one gene, preferably more than one gene, and most preferably all or nearly all of the genes in Tables 1-5.

Use of the BPH Markers for Drug Screening

[0075] According to the present invention, the genes identified in Tables 1-5 can be used as markers to screen for potential therapeutic agents or compounds to treat BPH or prostate cancer. A candidate drug or agent can be screened for the ability to stimulate the transcription or expression of a given marker or to down-regulate or counteract the transcription or expression of a marker or markers. Compounds that modulate the expression level of single gene and also compounds that modulate the expression level of multiple genes from levels associated with a specific disease state to a normal state can be screened by using the markers and profiles identified herein.

[0076] According to the present invention, one can also compare the specificity of drug's effects by looking at the number of markers which are differentially expressed after drug exposure and comparing them. More specific drugs will have less transcriptional targets. Similar sets of markers identified for two drugs may indicate a similarity of effects.

[0077] Assays to monitor the expression of a marker or markers as defined in Tables 1-5 may utilize any available means of monitoring for changes in the expression level of the nucleic acids of the invention. As used herein, an agent is said to modulate the expression of a nucleic acid of the invention if it is capable of up- or down-regulating expression of the nucleic acid in a cell.

[0078] In one assay format, gene chips containing probes to at least 2 genes from Tables 1-5 may be used to directly monitor or detect changes in gene expression in the treated or exposed cell as described in more detail above. In another format, the changes of mRNA expression level can be detected using QuantiGene technology (Warrior *et. al.* (2000) *J. Biomolecular Screening*, 5, 343-351). Specific probes used for QuantiGene can be designed and synthesized to one or more genes from Tables 1-5. Cells treated with compounds are lysed by lysis buffer. The amount of target mRNA can be detected as a luminescence intensity using target specific probes.

[0079] In another format, cell lines that contain reporter gene fusions between the open reading frame and/or 5'/3' regulatory regions of a gene in Tables 1-5 and any assayable fusion partner may be prepared. Numerous assayable fusion partners are known and readily available including the firefly luciferase gene and the gene encoding chloramphenicol acetyltransferase (Alam *et al.* (1990) *Anal. Biochem.* 188:245-254). Cell lines containing the reporter gene fusions are then exposed to the agent to be tested under appropriate conditions and time. Differential expression of the reporter gene between samples exposed to the agent and control samples identifies agents which modulate the expression of the nucleic acid.

[0080] Additional assay formats may be used to monitor the ability of the agent to modulate the expression of a gene identified in Tables 1-5. For instance, as described above, mRNA

expression may be monitored directly by hybridization of probes to the nucleic acids of the invention. Cell lines are exposed to the agent to be tested under appropriate conditions and time and total RNA or mRNA is isolated by standard procedures such those disclosed in Sambrook *et al.* (*Molecular Cloning: A Laboratory Manual*, 2nd Ed. Cold Spring Harbor Laboratory Press, 1989).

[0081] In another assay format, cells or cell lines are first identified which express the gene products of the invention physiologically (see below). Cell and/or cell lines so identified would be expected to comprise the necessary cellular machinery such that the fidelity of modulation of the transcriptional apparatus is maintained with regard to exogenous contact of agent with appropriate surface transduction mechanisms and/or the cytosolic cascades. Such cell lines may be, but are not required to be, prostate derived. Further, such cells or cell lines may be transduced or transfected with an expression vehicle (*e.g.*, a plasmid or viral vector) construct comprising an operable non-translated 5'-promoter containing end of the structural gene encoding the instant gene products fused to one or more antigenic fragments, which are peculiar to the instant gene products, wherein said fragments are under the transcriptional control of said promoter and are expressed as polypeptides whose molecular weight can be distinguished from the naturally occurring polypeptides or may further comprise an immunologically distinct tag or some other detectable marker or tag. Such a process is well known in the art (see Maniatis).

[0082] Cells or cell lines transduced or transfected as outlined above are then contacted with agents under appropriate conditions; for example, the agent comprises a pharmaceutically acceptable excipient and is contacted with cells comprised in an aqueous physiological buffer such as phosphate buffered saline (PBS) at physiological pH, Eagles balanced salt solution (BSS) at physiological pH, PBS or BSS comprising serum or conditioned media comprising PBS or BSS and/or serum incubated at 37°C. Said conditions may be modulated as deemed necessary by one of skill in the art. Subsequent to contacting the cells with the agent, said cells are disrupted and the polypeptides of the lysate are fractionated such that a polypeptide fraction is pooled and contacted with an antibody to be further processed by immunological assay (*e.g.*, ELISA, immunoprecipitation or Western blot). The pool of proteins isolated from the "agent-contacted" sample is then compared with a control sample where only the excipient is contacted with the cells and an increase or decrease in the immunologically generated signal from the "agent-contacted" sample compared to the control is used to distinguish the effectiveness of the agent.

[0083] Another embodiment of the present invention provides methods for identifying agents that modulate at least one activity of a protein(s) encoded by the genes in Tables 1-5. Such methods or assays may utilize any means of monitoring or detecting the desired activity.

[0084] In one format, the relative amounts of a protein of the invention between a cell population that has been exposed to the agent to be tested compared to an un-exposed control cell population may be assayed. In this format, probes such as specific antibodies are used to monitor the differential expression of the protein in the different cell populations. Cell lines or populations are exposed to the agent to be tested under appropriate conditions and time. Cellular lysates may be prepared from the exposed cell line or population and a control, unexposed cell line or population. The cellular lysates are then analyzed with the probe, such as a specific antibody.

[0085] Agents that are assayed in the above methods can be randomly selected or rationally selected or designed. As used herein, an agent is said to be randomly selected when the agent is chosen randomly without considering the specific sequences involved in the association of the a protein of the invention alone or with its associated substrates, binding partners, *etc.* An example of randomly selected agents is the use a chemical library or a peptide combinatorial library, or a growth broth of an organism.

[0086] As used herein, an agent is said to be rationally selected or designed when the agent is chosen on a nonrandom basis which takes into account the sequence of the target site and/or its conformation in connection with the agent's action. Agents can be rationally selected or rationally designed by utilizing the peptide sequences that make up these sites. For example, a rationally selected peptide agent can be a peptide whose amino acid sequence is identical to or a derivative of any functional consensus site.

[0087] The agents of the present invention can be, as examples, peptides, small molecules, vitamin derivatives, as well as carbohydrates. Dominant negative proteins, DNAs encoding these proteins, antibodies to these proteins, peptide fragments of these proteins or mimics of these proteins may be introduced into cells to affect function. "Mimic" used herein refers to the modification of a region or several regions of a peptide molecule to provide a structure chemically different from the parent peptide but topographically and functionally similar to the parent peptide (see Grant GA. in: Meyers (ed.) Molecular Biology and Biotechnology (New York, VCH Publishers, 1995), pp. 659-664). A skilled artisan can readily recognize that there is no limit as to the structural nature of the agents of the present invention.

Cells used for Multi Gene Screening

[0088] Many kinds of cells such as primary cells and cell lines can be used for the drug screening methods of the invention. Cells or cell lines derived from prostatic tissues are preferred because the innate gene expression mechanisms of these cells often resemble those of prostatic tissues. Cells used for drug screening can be selected by assaying for the expression of one or more of the marker genes listed in Tables 1-5. The cells which differentially express one or more, or preferably nearly all of the marker genes listed in Tables 1-5 are preferred cells or cell lines for the methods of the invention (see Table 6).

Kits

[0089] The invention further includes kits combining, in different combinations, high-density oligonucleotide arrays, reagents for use with the arrays, signal detection and array-processing instruments, gene expression databases and analysis and database management software described above. The kits may be used, for example, to diagnose the disease state of a tissue or cell sample, to monitor the progression of prostate disease states, to identify genes that show promise as new drug targets and to screen known and newly designed drugs as discussed above.

[0090] The databases packaged with the kits are a compilation of expression patterns from human and laboratory animal genes and gene fragments (corresponding to the genes of Tables 1-5). In particular, the database software and packaged information include the expression results of Tables 1-5 that can be used is the assays and methods as herein described.

[0091] The kits may used in the pharmaceutical industry, where the need for early drug testing is strong due to the high costs associated with drug development, but where bioinformatics, in particular gene expression informatics, is still lacking. These kits will reduce the costs, time and risks associated with traditional new drug screening using cell cultures and laboratory animals. The results of large-scale drug screening of pre-grouped patient populations, pharmacogenomics testing, can also be applied to select drugs with greater efficacy and fewer side-effects. The kits may also be used by smaller biotechnology companies and research institutes who do not have the facilities for performing such large-scale testing themselves.

[0092] Databases and software designed for use with use with microarrays is discussed in Balaban *et al.*, U.S. Patent Nos. 6,229,911, a computer-implemented method for managing information, stored as indexed tables, collected from small or large numbers of microarrays, and 6,185,561, a computer-based method with data mining capability for collecting gene expression

level data, adding additional attributes and reformatting the data to produce answers to various queries. Chee *et al.*, U.S. Patent No. 5,974,164, disclose a software-based method for identifying mutations in a nucleic acid sequence based on differences in probe fluorescence intensities between wild type and mutant sequences that hybridize to reference sequences

[0093] Without further description, it is believed that one of ordinary skill in the art can, using the preceding description and the following illustrative examples, make and utilize the genes, chips, *etc.* of the present invention and practice the claimed methods. The following working examples therefore, specifically point out the preferred embodiments of the present invention, and are not to be construed as limiting in any way the remainder of the disclosure.

EXAMPLES

Example 1: Gene chip expression analysis

[0094] BPH, normal prostate tissue, and prostate tissue adjacent to malignant prostate tissue were obtained from human biopsy samples.

[0095] Microarray sample preparation was conducted with minor modifications, following the protocols set forth in the Affymetrix GeneChip Expression Analysis Manual. Frozen tissue was ground to a powder using a Spex Certiprep 6800 Freezer Mill. Total RNA was extracted with Trizol (GibcoBRL) utilizing the manufacturer's protocol. The total RNA yield for each sample was 200-500 μg per 300 mg tissue weight. mRNA was isolated using the Oligotex mRNA Midi kit (Qiagen) followed by ethanol precipitation. Double stranded cDNA was generated from mRNA using the SuperScript Choice system (GibcoBRL). First strand cDNA synthesis was primed with a T7-(dT24) oligonucleotide. The cDNA was phenol-chloroform extracted and ethanol precipitated to a final concentration of 1 μg/ml. From 2 μg of cDNA, cRNA was synthesized using Ambion's T7 MegaScript *in vitro* Transcription Kit.

[0096] To biotin label the cRNA, nucleotides Bio-11-CTP and Bio-16-UTP (Enzo Diagnostics) were added to the reaction. Following a 37°C incubation for six hours, impurities were removed from the labeled cRNA following the RNeasy Mini kit protocol (Qiagen). cRNA was fragmented (fragmentation buffer consisting of 200 mM Tris-acetate, pH 8.1, 500 mM KOAc, 150 mM MgOAc) for thirty-five minutes at 94°C. Following the Affymetrix protocol, 55 μg of fragmented cRNA was hybridized on the Affymetrix Human 42K array set for twenty-four hours at 60 rpm in a 45°C hybridization oven. The chips were washed and stained with Streptavidin Phycoerythrin (SAPE) (Molecular Probes) in Affymetrix fluidics stations. To amplify staining,

SAPE solution was added twice with an anti-streptavidin biotinylated antibody (Vector Laboratories) staining step in between. Hybridization to the probe arrays was detected by fluorometric scanning (Hewlett Packard Gene Array Scanner). Data was analyzed using Affymetrix GeneChip version 3.0 and Expression Data Mining Tool (EDMT) software (version 1.0).

[0097] Differential expression of genes between the BPH and normal prostate samples were determined using the Affymetrix GeneChip human gene chip set by the following criteria: 1) For each gene, Affymetrix GeneChip average difference values were determined by standard Affymetrix EDMT software algorithms, which also made "Absent" (=not specifically detected as gene expression), "Present" (=detected) or "Marginal" (=not clearly Absent or Present) calls for each GeneChip element; 2) all AveDiff values which were less than +20 (positive 20) were raised to a floor of +20 so that fold change calculations could be made where values were not already greater than or equal to +20; 3) median levels of expression were compared between the normal control group and the BPH with symptoms disease group to obtain greater than or equal 2-fold up/down values; 4) The median value for the higher expressing group needed to be greater or equal to 200 average difference units in order to be considered for statistical significance; 5) Genes passing the criteria of #1-4 were analyzed for statistical significance using a two-tailed T test and deemed statistically significant if $p < 0.05$. Tables 1 and 2 list the genes and their levels of differential expression (compared to normal samples) in BPH tissue from patients with symptoms of BPH and in BPH tissue immediately adjacent to malignant prostate tissue isolated from male patients.

Example 2 : Expression profile analysis

[0098] Gene expression profiles between normal sample and BPH patient samples were determined by using the following samples: 10 normal; 7 BPH without symptoms; 8 BPH with cancer; and 8 BPH with symptoms. Gene expression profiles were prepared using the 42K Affymetrix Gene Chip set. The methods used were the same as described in Example 1 with the exception of the criteria to select the marker genes.

[0099] The criteria used in this study were as follows; 1) For each gene, Affymetrix GeneChip average difference values were determined by standard Affymetrix EDMT software algorithms, which also made "Absent" (=not specifically detected as gene expression), "Present" (=detected) or "Marginal" (=not clearly Absent or Present) calls for each GeneChip element; 2) all AveDiff

values which were less than +20 (positive 20) were raised to a floor of +20 so that fold change calculations could be made where values were not already greater than or equal to +20; 3) mean levels of expression were compared between the normal control group and the BPH with symptoms disease group; 4) genes were arranged by the fold change starting with the largest one (Fold change calculation was determined by using logarithmic values in Example 2); and 5) the top 200 up-regulated genes and bottom 200 down-regulated genes were selected. The genes identified in this study are listed in Tables 3 (normal vs. BPH with symptoms, up regulated) and 4 (normal vs. BPH with symptoms, down regulated, values are negative fold-change from normal).

Example 3 : Selection of Cell lines used for Multi Gene Screening

[0100] A number of cultured cell lines were tested to determine the similarity in gene expression profiles to BPH tissue. Cells were cultured in 6-well plates using the appropriate medium for each cell line. After reaching 90% confluency, cells were lysed with Trizol (GiboBRL) and total RNA was extracted. mRNA was then isolated, cDNA and cRNA was synthesized, and gene expression levels were determined by the Affymetrix Human 42K Gene Chip set as described in more detail above.

[0101] The gene expression profiles were compared with those of prostatic tissue samples. A panel of 61 genes whose expression levels were up-regulated in BPH with symptoms compared with normal samples and with small variation among samples (within BPH samples and within normal samples) were assayed. The number of genes whose signal intensity was more than 100 in each cell line is summarized in Table 6. A panel of 43 genes whose expression levels were down-regulated in BPH patient with small variation among samples was also assayed. The number of genes whose signal intensity in Affymetrix Gene Chip was "Present call" is also included in Table 6.

[0102] Forty-eight to 58% of genes applied for this analysis were expressed in the cell lines of Table 6. These results indicate that cell lines, BRF-55T (Biological Research Faculty & Facility Inc.), PZ-HPV7 (ATCC; CRL-2221) , BPH-1 (S.W. Hayward *et al.*, *In Vitro Cell Dev. Biol.* 31A, 14-24, 1995) and LNCaP (ATCC; CRL-1740) can be used as a BPH – like cell population to screen for compounds which are capable of modulating gene expression profiles from the disease state to a normal state. In particular, BRF-55T is a useful cell line for screening in the assays of

the invention, because 58% genes of the assayed genes were differentially expressed in BRF-55T as compared to BPH with symptoms tissue.

Example 4 : Cluster analysis of up- or down-regulated genes in BPH

[0103] Cluster analysis of the expression results from a large number of genes is often problematic due to variations in the standardization of the gene expression data. To compensate for these variations, a subset of differentially expressed genes was selected by a modified analysis procedure.

[0104] In a first step, a gene list comparing normal vs. disease samples was generated by two kinds of comparisons. First, genes were selected that displayed a greater than or equal to mean 2-fold up or down regulation using average difference expression values and with $p<0.05$. Second, genes were selected by ANOVA comparing the normal group of samples with the disease group and with a t value of >3 in the up or down direction. These lists were then combined to create an expression profile characteristic of normal controls and one characteristic of disease in which specific genes are found to be up or down regulated in disease when compared with normal controls.

[0105] In preparation for clustering analysis to identify subgroups of genes that show statistically similar expression patterns, average difference values for the selected genes were normalized across all samples (normal and disease combined) using the following formula:

Normalization data = (X - Xmean)/Sx

Where Sx is variance (:STD)

[0106] This converts the mean expression value for each gene to 0 and the high and low values to 1 and –1, respectively. Thus, genes with high absolute expression values when compared with genes with low absolute expression values would not skew the comparisons when clustering algorithms are applied.

[0107] The measurement of the cluster space distance was determined by using the correlation coefficient (1-r) method and clustering was performed using Ward's method (Ward,J.H. (1963) *Journal of American Statistical Association*, 58. 236.)

[0108] The clustering was validated by observing whether multiple elements representing the same genes showing the same direction of expression change (*i.e.*, either up or down) tend to cluster together. To test this standardization and clustering protocol, the expression levels for genes that are represented by more than one element on the 42K gene chip set were analyzed to

determine whether the multiple elements for a single gene could be clustered together. For example, tryptase, also known as alpha tryptase or beta (tryptase II) is represented by two separate elements on the 42K human gene chip. This gene is registered with 2 different element names 41268 (5), M33493_s_at (code name, Up-170) and 26389 (3), rc_AA131322_s_at (code name, Up-010).

[0109] It was found that the best analysis means for decreasing measurement errors between these two elements is by the Ward method as it gave the most consistent results when compared to other clustering methods. These analysis methods may be incorporated into software or computer readable storage media for storing a computer programmer software.

Example 5 : Selection of 60 Marker Genes

[0110] A panel of 60 representative marker genes (listed in Table 5) out of 400 marker genes listed in Tables 3 and 4 can be used in the assays and methods of the invention. The 60 marker genes were selected based on following criteria: (1) expression level is changed greatly in BPH patient samples compared with normal samples; (2) variation of expression levels within BPH samples and within normal samples is small; and (3) expression levels resembling BPH with symptoms are detected in cell line BRF-55T.

Example 6: Gene Expression Analysis of Select Genes

[0111] The expression levels of three genes from Tables 1-5 (the genes encoding cellular retinol binding protein, S100 calcium binding protein and PSMA) were assayed in various tissues and prostate samples by PCR as described in Example 7 (see Figures 1-6). Each sample was assayed for the level of GAPDH and mRNA corresponding to cellular retinol binding protein, S100 calcium binding protein or PSMA. As seen in Figures 1-6, these three genes are differentially regulated or expressed in BPH tissue from patients with or without symptoms and from BPH tissue from patients with prostate cancer (compared to normal prostate tissue). All three genes are therefore useful markers in the assays of the invention, such as the assays to measure the effect of an agent on BPH or the assays to detect or diagnose the occurrence or progression of BPH.

Example 7: Drug Screening Assays

[0112] The expression profiles for normal controls and disease samples described above can be used to identify compound hits from a compound library. A hit may be defined as one of three kinds of results:

[0113] 1) The expression of an individual gene is changed in the direction of normal (*i.e.*, if up in disease, then down=hit, if down in disease, then up=hit). The stronger the modulation of an individual gene to a normal phenotype, the stronger the hit status for the compound against that gene.

[0114] 2) The expression of genes that subcluster together is evaluated for an overall pattern of modulation to a normal expression profile. The more genes in a subcluster that are modulated to a normal phenotype, the stronger the hit status for the compound against that subcluster. A subcluster may represent common or interacting cellular pathways.

[0115] 3) The overall expression profile of all of the genes being screened is evaluated for modulation to normal. The more genes that are modulated to a normal phenotype, the stronger the hit status for the compound against the entire gene set.

[0116] As described above, if a compound modulates the gene expression pattern of the screening system cells more towards any disease phenotype, then it can be used as a molecular probe to find binding proteins and/or define disease-associated cellular pathways.

[0117] As an example, candidate agents and compounds are screened for their ability to modulate the expression levels of cellular retinol binding protein, S100 calcium binding protein and PSMA by exposing a prostate cell line or cell line from BPH tissue to the agent and assaying the expression levels of these genes by real time PCR. Real time PCR detection is accomplished by the use of the ABI PRISM 7700 Sequence Detection System. The 7700 measures the fluorescence intensity of the sample each cycle and is able to detect the presence of specific amplicons within the PCR reaction. Each sample is assayed for the level of GAPDH and mRNA corresponding to cellular retinol binding protein, S100 calcium binding protein and PSMA. GAPDH detection is performed using Perkin Elmer part#402869 according to the manufacturer's directions. Primers were designed for the three genes by using Primer Express, a program developed by PE to efficiently find primers and probes for specific sequences ((1) N91971 - FAM PROBE Forward: 5'- CAT ggC TTT gTT TTA AgA AAA ggA A -3'; Reverse: 5'- AgC CAC CCC CAg gCA T -3'; Probe: 5'-FAM - AgT gAC AAA gCC AAg AgA CAg ACT CTg CTA ACA - TAMRA-3'; (2) X65614 – SYBR; Forward: 5'- AAA gAC AAg gAT gCC gTg gAT -3'; Reverse 5'-AgC CAC gAA CAC gAT gAA CTC-3'; (3) M99487-SYB; Forward 5'-Tgg CTC AgC ACC ACC Aga T-3'; Reverse: 5'-TTC Cag TAA AgC Cag gTC CAA-3')

[0118] These primers are used in conjunction with SYBR green (Molecular Probes), a nonspecific double stranded DNA dye, to measure the expression level mRNA corresponding to the genes, which is normalized to the GAPDH level in each sample.

[0119] Normalized expression levels from cells exposed to the agent are then compared to the normalized expression levels in control cells. Agents that modulate the expression of one or more the genes may be further tested as drug candidates in appropriate BPH *in vitro* or *in vivo* models.

Example 8 Diagnostic assays

[0120] The expression profiles or one or more of the individual genes of Tables 1-5 are used as molecular or diagnostic markers to evaluate the disease status of a patient sample. In one embodiment, a patient prostate tissue sample is processed as described herein to produce total cellular or mRNA. The RNA is hybridized to a chip continuing probes that specifically hybridize to one or more, or two or more of the genes in Tables 1-5. The overall expression profile generated, or the expression levels of individual genes are then compared to the profiles as described in Tables 1-5 to determine the disease or hyperplastic state of the patient sample.

[0121] Although the present invention has been described in detail with reference to examples above, it is understood that various modifications can be made without departing from the spirit of the invention. Accordingly, the invention is limited only by the following claims. All cited patents, applications, GenBank Accession numbers and publications referred to in this application are herein incorporated by reference in their entirety.

Normal1-Normal2 vs BPH-With Symptoms Table **TABLE 1**

	Affy element	Genbank ID	Genbank Name	Fold-change N1-N2 vs With	p-value N1-N2 vs With
up-regulated	RC_AA410383_at	AA410383	B-cell-homing chemokine (ligand for Burkitt's lymphoma receptor-1)4q21	22.5	0.025197485
	RC_AA463726_s_at	AA463726	JM27 proteinXp11.23	14.9	0.018598344
	RC_AA057195_at	AA057195	Homo sapiens mRNA; cDNA DKFZp586M121 (from clone DKFZp586M121)	14.0	0.029325045
	V01512_rna1_at	V01512_rna1	v-fos FBJ murine osteosarcoma viral oncogene homolog14q24.3	13.1	0.001027561
	RC_AA427622_s_at	AA427622	collagen, type XIII, alpha 110q22	11.6	0.00074954
	RC_N23730_s_at	N23730	v-fos FBJ murine osteosarcoma viral oncogene homolog14q24.3	11.4	0.000631487
	RC_AA465491_at	AA465491	Mad4 homolog4p16.3	11.4	0.031024189
	RC_AA620825_at	AA620825	ESTs	11.3	0.010915901
	RC_R93908_at	R93908	ESTs	11.3	0.019994337
	RC_AA461300_at	AA461300	ESTs	11.0	0.007061759
	N40141_at	N40141	JM27 proteinXp11.23	10.9	0.013756347
	RC_R25410_at	R25410	ESTs	7.7	0.01851753
	L49169_at	L49169	FBJ murine osteosarcoma viral oncogene homolog B19q13.3	7.4	0.041523744
	RC_AA279760_at	AA279760	ESTs	7.0	0.024411468
	RC_T90889_at	T90889	ESTs	6.5	0.015666863
	U62015_at	U62015	insulin-like growth factor binding protein 101p22-p31	6.0	0.002843661
	RC_AA188981_at	AA188981	highly expressed in cancer, rich in leucine heptad repeats	5.9	0.002280479
	D83018_at	D83018	nel (chicken)-like 212q13.11-q13.12	5.6	0.000570952
	RC_H64493_f_at	H64493	immunoglobulin gamma 3 (Gm marker)14q32.33	5.6	0.01109802
	X52541_at	X52541	early growth response 15q31.1	5.2	0.002428259
	M57466_s_at	M57466	major histocompatibility complex, class II, DP beta 16p21.3	5.1	0.002137399
	J03507_at	J03507	complement component 75p13	4.9	1.36616E-05
	RC_N30198_at	N30198	ESTs	4.8	0.003366461
	RC_T78398_at	T78398	EST	4.8	0.033293747
	RC_H17550_at	H17550	ESTs	4.7	0.047828622
	RC_T67053_f_at	T67053	immumoglobulin lambda gene cluster22q11.1-q11.2	4.5	0.045107075
	RC_AA598982_s_at	AA598982	trophininXp11.22-p11.21	4.3	0.000902336
	RC_AA256268_at	AA256268	ESTs	4.2	0.001506239
	HG3543-HT3739_at	M29645	insulin-like growth factor 2 (somatomedin A)11p15.5	4.1	0.017253126
	RC_N91971_f_at	N91971	retinol-binding protein 1, cellular3q23	4.1	0.02528773
	RC_AA479286_at	AA479286	ESTs	4.0	0.028009544
	M62831_at	M62831	immediate early protein19	4.0	0.000484086
	RC_F02992_at	F02992	ESTs, Weakly similar to unknown [M.musculus]	3.9	0.031845412
	RC_H86112_f_at	H86112	KIAA0471 gene product1q24-q25	3.8	0.004155259
	RC_AA436616_at	AA436616	ESTs	3.8	0.017156387
	RC_T62857_at	T62857	ESTs	3.7	0.000301735

Normal1-Normal2 vs BPH-With Symptoms Table **TABLE 1**

Affy element	Genbank ID	Genbank Name	Fold-change N1-N2 vs With	p-value N1-N2 vs With
RC_AA281345_f_at	AA281345	immediate early protein19	3.6	0.001679723
U21128_at	U21128	lumican12q21.3-q22	3.6	2.19529E-05
U30521_at	U30521	P311 protein	3.6	0.001150397
RC_N58172_at	N58172	ESTs	3.5	0.043092144
RC_T03229_f_at	T03229	EST	3.5	0.031101935
X06700_s_at	X06700	collagen, type III, alpha 1 (Ehlers-Danlos syndrome type IV, autosomal dominant	3.5	0.008472599
RC_Z39904_at	Z39904	Homo sapiens clone 23555 mRNA sequence	3.4	0.002949046
RC_T23622_at	T23622	ESTs	3.4	0.002174281
J00231_f_at	J00231	immunoglobulin gamma 3 (Gm marker)14q32.33	3.4	0.009322568
RC_AA028092_s_at	AA028092	transcription factor 216pter-qter	3.4	3.13963E-06
RC_AA252528_at	AA252528	ESTs	3.4	0.000225707
L33799_at	L33799	procollagen C-endopeptidase enhancer7q22	3.3	0.018469201
RC_F09748_s_at	F09748	Homo sapiens mRNA; cDNA DKFZp586K1220 (from clone DKFZp586K1220)	3.2	0.02728166
RC_T64223_s_at	T64223	carboxypeptidase A3 (mast cell)3q21-q25	3.2	0.027915742
RC_AA402903_f_at	AA402903	immunoglobulin gamma 3 (Gm marker)14q32.33	3.2	0.044721116
RC_F13763_at	F13763	ESTs	3.1	0.000503701
RC_AA488432_at	AA488432	phosphoserine phosphatase7p21-p15	3.1	0.020997503
RC_AA486072_i_at	AA486072	small inducible cytokine A5 (RANTES)17q11.2-q12	3.1	0.025877597
RC_N22006_s_at	N22006	EST	3.1	0.00148561
RC_AA257093_r_at	AA257093	T-cell receptor, beta cluster7q35	3.1	1.71945E-07
RC_AA609943_at	AA609943	ESTs	3.0	0.029360518
RC_T23490_s_at	T23490	ESTs	3.0	0.008741411
D13628_at	D13628	angiopoietin 18q22.3-q23	2.9	0.006228419
M73720_at	M73720	carboxypeptidase A3 (mast cell)3q21-q25	2.9	0.006585391
Z74616_s_at	Z74616	collagen, type I, alpha 27q22.1	2.8	0.008750622
AA082546_at	AA082546	ESTs	2.8	0.019771126
RC_AA284920_at	AA284920	ESTs	2.7	0.019738239
RC_AA599365_at	AA599365	decorin12q23	2.7	0.001295936
X57025_at	X57025	insulin-like growth factor 1 (somatomedin C)12q22-q23	2.7	0.022341194
X51345_at	X51345	jun B proto-oncogene19p13.2	2.7	0.036487159
RC_N67876_s_at	N67876	insulin-like growth factor 1 (somatomedin C)12q22-q23	2.7	0.035216134
RC_AA609504_at	AA609504	KIAA0405 gene product	2.7	0.020881055
RC_N69207_at	N69207	ESTs, Moderately similar to !!!! ALU SUBFAMILY SB2 WARNING ENTRY !!!! [H.	2.6	0.041315387
M87789_s_at	M87789	Immunoglobulin gamma 3 (Gm marker)14q32.33	2.6	0.038916248
HG3510-HT3704_at	X12795	nuclear receptor subfamily 2, group F, member 15q14	2.6	0.016151338
RC_T64211_at	T64211	ESTs, Weakly similar to pancortin-1 [M.musculus]	2.6	0.006233291

Normal1-Normal2 vs BPH-With Symptoms Table **TABLE 1**

Affy element	Genbank ID	Genbank Name	Fold-change N1-N2 vs With	p-value N1-N2 vs With
U90552_s_at	U90552	butyrophilin, subfamily 3, member A16p23	2.6	0.004564282
M34516_r_at	M34516	immunoglobulin lambda-like polypeptide 322q11.2	2.6	0.049767038
RC_T23468_at	T23468	ESTs	2.5	0.00250737
RC_AA173223_at	AA173223	ESTs, Weakly similar to !!!! ALU SUBFAMILY SQ WARNING ENTRY !!!! [H.sapi	2.5	0.007080285
RC_T49061_at	T49061	ESTs	2.5	0.039642391
RC_AA234095_at	AA234095	ESTs	2.5	0.003152859
RC_F01920_s_at	F01920	pre-B-cell leukemia transcription factor 39q33-q34	2.5	0.002088945
RC_N91461_at	N91461	ESTs	2.4	0.01015467
RC_N67575_s_at	N67575	osteoglycin (osteoinductive factor)	2.4	0.004044061
RC_AA151210_at	AA151210	ESTs	2.4	0.011476541
AA156897_s_at	AA156897	Homo sapiens mRNA; cDNA DKFZp564I1922 (from clone DKFZp564I1922)	2.4	0.033974981
W73859_at	W73859	transcription factor 216pter-qter	2.4	0.024640626
RC_H68097_at	H68097	EST	2.4	0.04870874
RC_AA436618_at	AA436618	ESTs	2.4	0.02483165
M33493_s_at	M33493	tryptase, beta (tryptase II)16p13.3	2.4	0.02689938
AB002340_at	AB002340	KIAA0342 gene product	2.3	0.000748796
RC_AA446661_at	AA446661	ESTs	2.3	0.011980248
RC_AA084138_at	AA084138	ESTs	2.3	1.16025E-05
RC_N59866_at	N59866	ESTs, Weakly similar to putative p150 [H.sapiens]	2.3	0.002042263
RC_R42424_at	R42424	ESTs	2.3	0.003173074
RC_N39415_at	N39415	osteoglycin (osteoinductive factor)	2.3	0.001310764
J03464_s_at	J03464	collagen, type I, alpha 27q22.1	2.3	0.006791534
RC_AA205376_at	AA205376	KIAA0471 gene product1q24-q25	2.3	0.023123837
RC_H95960_at	H95960	secreted protein, acidic, cysteine-rich (osteonectin)5q31.3-q32	2.3	0.008509182
D28137_at	D28137	bone marrow stromal cell antigen 219p13.2	2.3	0.031127266
RC_N79778_at	N79778	extracellular matrix protein 2, female organ and adipocyte specific9q22.3	2.3	0.045073744
RC_N98485_s_at	N98485	forkhead (Drosophila)-like 66p25.3	2.3	0.033372862
M98539_at	M98539	prostaglandin D2 synthase (21kD, brain)9q34.2-q34.3	2.2	0.005442674
RC_AA205724_at	AA205724	ESTs	2.2	0.006183612
U85625_at	U85625	Homo sapiens ribonuclease 6 precursor, mRNA, complete cds.	2.2	0.001245066
RC_R37588_s_at	R37588	RAB2, member RAS oncogene family-like6p21.3	2.2	0.00219386
RC_AA046426_at	AA046426	Cdc42 effector protein 3	2.2	0.005788723
RC_AA256294_at	AA256294	ESTs	2.2	0.002425605
RC_AA599120_at	AA599120	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, sub	2.2	0.042979241
RC_W60186_at	W60186	ESTs	2.2	0.028494835
RC_AA599216_at	AA599216	collapsin response mediator protein 14p16.1-p15	2.2	0.040523744

Normal1-Normal2 vs BPH-With Symptoms Table **TABLE 1**

Affy element	Genbank ID	Genbank Name	Fold-change N1-N2 vs With	p-value N1-N2 vs With
RC_AA450324_at	AA450324	ESTs	2.1	0.009094567
M31994_at	M31994	Homo sapiens aldehyde dehydrogenase (ALDH1) gene	2.1	0.001561218
RC_AA402930_at	AA402930	ESTs	2.1	0.000114627
M91029_cds2_at	M91029_cds2	Human AMP deaminase isoform L (AMPD2) mRNA, exons 6-18, partial cds	2.1	0.02494373
RC_AA450114_at	AA450114	ESTs, Weakly similar to 17beta-hydroxysteroid dehydrogenase [H.sapiens]	2.1	4.87556E-06
D62584_at	D62584	osteoglycin (osteoinductive factor)	2.1	0.000157116
RC_AA621634_at	AA621634	ESTs	2.1	0.02297009
RC_AA312946_s_at	AA312946	ESTs	2.1	3.51075E-05
X07438_s_at	X07438	Human DNA for cellular retinol binding protein (CRBP)	2.1	0.039015947
RC_N53447_at	N53447	integral membrane protein 2CXq21.1-21.2	2.1	0.009032297
RC_AA281591_at	AA281591	Homo sapiens mRNA; cDNA DKFZp586B211 (from clone DKFZp586B211)	2.0	0.016660714
RC_R71395_at	R71395	ESTs, Moderately similar to alternatively spliced product using exon 13A [H.sapi	2.0	0.046231847
RC_T53590_s_at	T53590	cytochrome P450, subfamily XIA (cholesterol side chain cleavage)15q23-q24	2.0	0.00282074
RC_AA293489_at	AA293489	KIAA0638 protein	2.0	0.006966532
RC_AA447707_s_at	AA447707	KIAA1055 protein	2.0	0.001248537
RC_AA235618_f_at	AA235618	ESTs	2.0	0.012481746
RC_N68350_at	N68350	ESTs	2.0	0.035156598
RC_H81379_s_at	H81379	ESTs, Moderately similar to KIAA0438 [H.sapiens]	2.0	0.01148429
RC_D51060_s_at	D51060	Jun activation domain binding protein1p32-p31	2.0	0.016668951
U72649_at	U72649	B-cell translocation gene 2 (pheochromacytoma cell-3)1q32	2.0	0.020660388
RC_AA287389_at	AA287389	ESTs	2.0	0.002741873
RC_AA621367_at	AA621367	ESTs	2.0	0.004871903
J03040_at	J03040	secreted protein, acidic, cysteine-rich (osteonectin)5q31.3-q32	2.0	0.006303994
RC_AA291676_s_at	AA291676	non-metastatic cells 5, protein expressed in (nucleoside-diphosphate kinase)5q2	2.0	0.027480479
RC_N63536_at	N63536	ESTs	2.0	0.000634305
RC_AA411952_at	AA411952	UDP-Gal:betaGlcNAc beta 1,3-galactosyltransferase, polypeptide 33q25	2.0	0.011858934
RC_AA252802_s_at	AA252802	Human mRNA for TI-227H	2.0	0.041027635
RC_AA382275_at	AA382275	ESTs	2.0	0.00087437
AA093923_at	AA093923	tissue inhibitor of metalloproteinase 217q25	2.0	0.046200886
M11313_s_at	M11313	alpha-2-macroglobulin12p13.3-p12.3	2.0	0.013660595
RC_AA398280_at	AA398280	ESTs	2.0	0.044320644
RC_N51529_at	N51529	ESTs	2.0	0.006276979
H49440_at	H49440	nudix (nucleoside diphosphate linked moiety X)-type motif 36p21.2	2.0	0.013879331
RC_T33263_s_at	T33263	KIAA0320 protein	2.0	0.009994615
RC_T89160_r_at	T89160	ESTs	2.0	0.005289266
RC_W56792_at	W56792	ESTs, Weakly similar to serine/threonine protein kinase TAO1 [R.norvegicus]	2.0	0.026130523

Normal1-Normal2 vs BPH-With Symptoms Table **TABLE 1**

	Affy element	Genbank ID	Genbank Name	Fold-change N1-N2 vs With	p-value N1-N2 vs With
	RC_R60056_at	R60056	ESTs, Moderately similar to alternatively spliced product using exon 13A [H.sapi	2.0	0.001585076
Down-regulated	RC_AA398908_at	AA398908	Human Chromosome 16 BAC clone CIT987SK-A-61E3	-21.7	0.007918174
	RC_AA460914_at	AA460914	ESTs	-15.8	0.013659536
	RC_T40895_at	T40895	ESTs	-12.6	0.002430219
	RC_R71792_s_at	R71792	ESTs, Moderately similar to FAT-SPECIFIC PROTEIN FSP27 [M.musculus]	-9.8	0.01438632
	RC_N80129_i_at	N80129	metallothionein 1L16q13	-8.7	0.002816872
	X66141_at	X66141	myosin, light polypeptide 2, regulatory, cardiac, slow12q23-q24.3	-8.0	0.03928942
	AA234634_f_at	AA234634	CCAAT/enhancer binding protein (C/EBP), delta8p11.2-p11.1	-7.4	0.000589696
	U78294_at	U78294	arachidonate 15-lipoxygenase, second type	-6.8	0.017271608
	RC_AA457566_at	AA457566	ESTs	-6.6	0.029644622
	X93036_at	X93036	phospholemman-like, expressed in breast tumors, 8kD	-6.2	0.011323909
	X57129_at	X57129	H1 histone family, member 26p21.3	-6.1	0.004161922
	HG1067-HT1067_r_at	M22406	Human intestinal mucin mRNA, partial cds, clone SMUC 42	-5.8	0.007202185
	X65614_at	X65614	S100 calcium-binding protein P4p16	-5.8	0.006892572
	RC_AA609006_at	AA609006	ESTs	-5.7	0.015701354
	J03910_rna1_at	J03910_rna1	metallothionein 1G16q13	-5.7	0.003506953
	RC_H94471_at	H94471	occludin5q13.1	-5.6	0.025014274
	AB000584_at	AB000584	prostate differentiation factor	-5.4	0.003235425
	RC_W88568_at	W88568	glycogenin 2Xp22.3	-5.1	0.048573115
	V00594_at	V00594	metallothionein 2A16q13	-5.0	0.000721258
	RC_T73433_s_at	T73433	angiotensinogen1q41-qter	-4.9	0.012700144
	RC_N94303_at	N94303	ESTs	-4.5	4.88059E-05
	RC_AA419011_at	AA419011	Homo sapiens mRNA; cDNA DKFZp586D0823 (from clone DKFZp586D0823)	-4.1	0.013801595
	RC_N32748_at	N32748	ESTs	-4.1	0.018749207
	RC_AA053424_at	AA053424	ESTs, Weakly similar to mucin Muc3 [R.norvegicus]	-4.0	0.001235197
	RC_AA599331_at	AA599331	ESTs	-4.0	0.005480655
	M99487_at	M99487	folate hydrolase (prostate-specific membrane antigen) 11p11.2	-3.9	0.013268152
	RC_F02245_at	F02245	monoamine oxidase AXp11.4-p11.3	-3.8	0.002950391
	X76717_at	X76717	metallothionein 1L16q13	-3.7	0.000868707
	X64177_f_at	X64177	metallothionein 1H16q13	-3.7	0.002089771
	RC_AA599522_r_at	AA599522	squamous cell carcinoma antigen recognised by T cells	-3.6	0.012643918
	L77701_at	L77701	human homolog of yeast mitochondrial copper recruitment gene	-3.6	0.003341007
	RC_D11824_at	D11824	ESTs, Moderately similar to weak similarity to Arabidopsis thaliana ubiquitin-like	-3.6	0.000803294
	RC_AA410311_at	AA410311	ESTs	-3.5	0.001234064
	RC_AA457235_at	AA457235	ESTs	-3.5	0.012177965

Normal1-Normal2 vs BPH-With Symptoms Table **TABLE 1**

Affy element	Genbank ID	Genbank Name	Fold-change N1-N2 vs With	p-value N1-N2 vs With
RC_N93798_at	N93798	protein tyrosine phosphatase type IVA, member 3	-3.5	0.007340453
RC_AA416762_s_at	AA416762	nuclear receptor subfamily 1, group H, member 219q13.3-19q13.3	-3.5	0.010404304
RC_F03969_at	F03969	ESTs, Weakly similar to tumorous Imaginal discs protein Tid56 homolog [H.sapie	-3.5	0.011826812
RC_AA045487_at	AA045487	ESTs	-3.4	0.025187615
RC_Z38744_at	Z38744	putative gene product13	-3.4	2.30674E-05
RC_N92502_s_at	N92502	ESTs, Moderately similar to HERV-E integrase [H.sapiens]	-3.4	0.02301359
RC_R91484_at	R91484	ESTs	-3.4	8.2306E-05
RC_AA165313_at	AA165313	ESTs	-3.3	0.028364404
RC_AA182030_at	AA182030	ESTs	-3.3	0.019770486
RC_T94447_s_at	T94447	ESTs, Moderately similar to (defline not available 4335935) [M.musculus]	-3.3	0.001427294
RC_W20486_f_at	W20486	ESTs	-3.3	0.002892697
RC_R16983_at	R16983	ESTs	-3.2	0.000912559
RC_AA504805_s_at	AA504805	interferon stimulated gene (20kD)15q26	-3.2	0.003905701
RC_T90190_s_at	T90190	H1 histone family, member 26p21.3	-3.2	0.020618793
RC_AA135870_at	AA135870	ESTs	-3.1	0.04609197
RC_H99035_at	H99035	ESTs	-3.1	0.000191451
RC_R28370_at	R28370	ESTs	-3.1	0.024606319
RC_T40995_f_at	T40995	alcohol dehydrogenase 3 (class I), gamma polypeptide4q21-q23	-3.1	0.024064044
MIP1-B_at	MIP1-B	karyopherin (importin) beta 2	-3.1	0.005882353
RC_AA447522_at	AA447522	ESTs, Highly simlar to differentially expressed in Fanconi anemia [H.sapiens]	-3.1	0.003518059
RC_AA461453_at	AA461453	ESTs, Moderately similar to Cab45a [M.musculus]	-3.0	0.021949087
AA429539_f_at	AA429539	ESTs	-3.0	0.017623102
RC_AA476944_at	AA476944	ESTs	-3.0	0.019974254
RC_N80129_f_at	N80129	metallothionein 1L16q13	-3.0	0.000219038
RC_N26904_at	N26904	ESTs, Weakly similar to FK506/rapamycin-binding protein FKBP13 precursor [H.	-2.9	0.006305062
RC_AA505136_at	AA505136	ESTs	-2.9	0.005400284
AA455001_s_at	AA455001	ESTs	-2.9	2.1534E-05
RC_W70131_at	W70131	ESTs	-2.9	0.005764635
RC_AA043349_at	AA043349	ESTs	-2.9	0.016983419
U02020_at	U02020	pre-B-cell colony-enhancing factor	-2.9	0.003324497
U52969_at	U52969	Purkinje cell protein 421q22.2-q22.3	-2.8	0.00078638
RC_H22453_at	H22453	ESTs	-2.8	0.000410695
RC_N22620_at	N22620	ESTs	-2.8	0.005507089
RC_N64683_at	N64683	ESTs	-2.8	0.00378977
RC_N24761_at	N24761	ESTs	-2.8	0.004837185
RC_AA464728_s_at	AA464728	ESTs	-2.8	0.004669897

Normal1-Normal2 vs BPH-With Symptoms Table **TABLE 1**

Affy element	Genbank ID	Genbank Name	Fold-change N1-N2 vs With	p-value N1-N2 vs With
RC_H83380_at	H83380	ESTs	-2.7	0.016543793
M30894_at	M30894	T-cell receptor, gamma cluster7p15-p14	-2.7	0.034153167
RC_H81070_f_at	H81070	Human metallothionein (MT)I-F gene	-2.7	0.022654931
J00073_at	J00073	actin, alpha, cardiac muscle15q11-qter	-2.7	0.029724167
RC_H05084_at	H05084	ESTs, Weakly similar to ORF YDL055c [S.cerevisiae]	-2.7	0.016965435
AA045870_at	AA045870	Homo sapiens mRNA; cDNA DKFZp564A072 (from clone DKFZp564A072)	-2.7	0.005480167
RC_T68873_f_at	T68873	metallothionein 1L16q13	-2.7	0.001140431
RC_N72253_at	N72253	ESTs	-2.7	0.001832591
RC_AA447977_s_at	AA447977	Homo sapiens mRNA; cDNA DKFZp564A072 (from clone DKFZp564A072)	-2.7	0.001255304
RC_H18947_at	H18947	ESTs	-2.7	0.00193501
RC_H77597_f_at	H77597	metallothionein 1H16q13	-2.7	0.001560766
RC_H94475_s_at	H94475	alpha-2-plasmin inhibitor17pter-p12	-2.6	0.01435663
RC_AA025370_at	AA025370	KIAA0872 protein	-2.6	0.013924142
RC_AA443114_at	AA443114	ESTs, Moderately similar to PIM-1 PROTO-ONCOGENE SERINE/THREONINE-	-2.6	0.000703574
RC_F09684_at	F09684	ESTs	-2.6	0.000107291
RC_AA031360_s_at	AA031360	ESTs	-2.6	0.047293081
RC_AA416685_at	AA416685	UNC13 (C. elegans)-like9p11-p12	-2.6	0.023296279
D29805_at	D29805	UDP-Gal:betaGlcNAc beta 1,4- galactosyltransferase, polypeptide 19p13	-2.6	2.3562E-05
RC_H58873_s_at	H58873	solute carrier family 2 (facilitated glucose transporter), member 11p35-p31.3	-2.5	0.000710917
M10942_at	M10942	metallothionein 1E (functional)16q13	-2.5	0.017370635
RC_T03593_at	T03593	ESTs	-2.5	0.006239127
RC_N95495_at	N95495	small inducible cytokine A5 (RANTES)17q11.2-q12	-2.5	0.002392984
RC_AA017063_r_at	AA017063	ESTs, Highly similar to Miz-1 protein [H.sapiens]	-2.5	0.048093776
RC_R00144_at	R00144	ESTs	-2.5	0.018222161
RC_AA599522_f_at	AA599522	squamous cell carcinoma antigen recognised by T cells	-2.5	0.03100833
RC_AA219552_s_at	AA219552	ESTs	-2.5	0.043156485
RC_AA447537_at	AA447537	ESTs, Moderately similar to (defline not available 5360237) [M.musculus]	-2.5	0.031129269
RC_AA070752_s_at	AA070752	insulin receptor substrate 12q36	-2.5	0.002895462
RC_R02003_r_at	R02003	ESTs, Weakly similar to cappuccino [D.melanogaster]	-2.4	0.002315115
L13698_at	L13698	growth arrest-specific 19q21.3-q22.1	-2.4	0.013393145
RC_AA432292_at	AA432292	ESTs, Moderately similar to B cell growth factor [H.sapiens]	-2.4	0.000956642
RC_H99648_s_at	H99648	DNA segment, single copy probe LNS-CAI/LNS-CAII (deleted in polyposis5q22-	-2.4	0.009066307
RC_AA131919_at	AA131919	putative type II membrane protein	-2.4	0.000187872
RC_AA621695_at	AA621695	ESTs	-2.4	0.008761556
RC_AA598695_at	AA598695	ESTs, Weakly similar to !!!! ALU SUBFAMILY SX WARNING ENTRY !!!! [H.sapi	-2.4	0.000549977
RC_AA430388_at	AA430388	ESTs, Moderately similar to !!!! ALU SUBFAMILY SQ WARNING ENTRY !!!! [H.	-2.4	0.000135176

Normal1-Normal2 vs BPH-With Symptoms Table **TABLE 1**

Affy element	Genbank ID	Genbank Name	Fold-change N1-N2 vs With	p-value N1-N2 vs With
M24069_at	M24069	cold shock domain protein A12p13.1	-2.4	0.015890231
RC_AA434108_at	AA434108	Homo sapiens heat shock protein hsp40-3 mRNA, complete cds	-2.4	0.013182623
RC_AA405488_at	AA405488	ESTs	-2.3	0.015044159
RC_AA419546_at	AA419546	ESTs	-2.3	0.030432017
RC_W38197_at	W38197	EST	-2.3	0.013006462
RC_R38709_s_at	R38709	superoxide dismutase 2, mitochondrial6q25.3	-2.3	0.03567491
RC_AA121142_at	AA121142	ESTs, Moderately similar to copper transport protein HAH1 [H.sapiens]	-2.3	0.043639016
RC_N26801_at	N26801	ESTs	-2.3	0.000580867
RC_N75960_at	N75960	ESTs	-2.3	0.01244791
RC_R36969_at	R36969	ESTs	-2.3	0.019129486
AA046840_at	AA046840	CCAAT/enhancer binding protein (C/EBP), delta8p11.2-p11.1	-2.3	0.002504544
RC_R46074_at	R46074	transforming, acidic coiled-coil containing protein 210q26	-2.3	0.003462273
X06956_at	X06956	tubulin, alpha 1 (testis specific)2q	-2.3	0.015437809
RC_H84761_s_at	H84761	glutathione peroxidase 13p21.3	-2.2	0.000365528
RC_W52065_f_at	W52065	KIAA0539 gene product	-2.2	0.016497348
RC_AA279757_at	AA279757	ESTs, Weakly similar to (defline not available 4481810) [D.melanogaster]	-2.2	0.003272622
RC_H16676_s_at	H16676	ESTs, Weakly similar to (defline not available 5107634) [R.norvegicus]	-2.2	8.86866E-05
RC_AA255480_at	AA255480	ESTs	-2.2	0.009359024
RC_R96924_s_at	R96924	ESTs	-2.2	0.000201685
RC_AA342337_at	AA342337	ESTs, Moderately similar to !!!! ALU SUBFAMILY SQ WARNING ENTRY !!!! [H.	-2.2	0.024999347
RC_AA004699_at	AA004699	putative translation initiation factor	-2.2	0.022298405
RC_AA401965_at	AA401965	tumor suppressor deleted in oral cancer-related 111q13	-2.2	0.006294885
RC_F02470_at	F02470	Homo sapiens clone 24796 mRNA sequence	-2.2	0.022313149
X76180_at	X76180	sodium channel, nonvoltage-gated 1 alpha12p13	-2.2	0.023078001
RC_R49138_s_at	R49138	coatomer protein complex, subunit epsilon	-2.2	0.020401578
RC_D80237_s_at	D80237	actin related protein 2/3 complex, subunit 4 (20 kD)	-2.2	0.022022634
RC_AA402224_at	AA402224	growth arrest and DNA-damage-inducible, gamma9q22.1-q22.2	-2.2	0.014983528
RC_AA281599_at	AA281599	Homo sapiens mRNA for for histone H2B, clone pjG4-5-14	-2.2	0.029567009
RC_N78630_at	N78630	KIAA0870 protein	-2.2	0.006668895
X85785_rna1_at	X85785_rna1	Duffy blood group1q21-q22	-2.2	0.018706507
RC_AA412063_at	AA412063	ESTs	-2.2	0.000686563
RC_AA022886_at	AA022886	ESTs, Weakly similar to phosphatidylinositol transfer protein [H.sapiens]	-2.2	0.000777067
RC_N24899_at	N24899	ESTs	-2.2	0.030610964
RC_AA101767_at	AA101767	ESTs	-2.2	0.009040467
RC_AA045503_at	AA045503	ESTs, Weakly similar to Homo sapiens p20 protein [H.sapiens]	-2.2	0.021950966
RC_F10078_at	F10078	ESTs	-2.1	0.040699115

Normal1-Normal2 vs BPH-With Symptoms Table **TABLE 1**

Affy element	Genbank ID	Genbank Name	Fold-change N1-N2 vs With	p-value N1-N2 vs With
RC_H02308_at	H02308	ESTs	-2.1	0.036730715
RC_AA284153_at	AA284153	ESTs	-2.1	0.021270233
RC_AA453433_at	AA453433	HLA-B associated transcript-16p21.3	-2.1	0.013366375
RC_AA403159_at	AA403159	Homo sapiens Ste-20 related kinase SPAK mRNA, complete cds	-2.1	0.025212073
RC_T17428_s_at	T17428	Homo saplens clone 23836 mRNA sequence	-2.1	0.044754602
RC_W92449_at	W92449	ESTs, Highly similar to (defline not available 4587714) [H.sapiens]	-2.1	0.019386585
RC_AA609312_at	AA609312	ESTs	-2.1	0.003204911
D28589_at	D28589	Human mRNA (KIAA00167), partial sequence	-2.1	0.000408478
RC_AA232508_at	AA232508	ESTs, Highly similar to (defline not available 4929647) [H.sapiens]	-2.1	0.004626663
RC_AA280929_s_at	AA280929	ESTs	-2.1	0.028189798
W63793_at	W63793	S-adenosylmethionine decarboxylase 16q21-q22	-2.1	0.032076011
RC_R36881_s_at	R36881	Homo sapiens DNA from chromosome 19-cosmid R30879 containing USF2, gen	-2.1	0.007343473
RC_AA278767_s_at	AA278767	ESTs	-2.1	0.001983494
RC_R98442_at	R98442	ESTs	-2.1	0.007227226
X99728_at	X99728	H.sapiens NDUFV3 gene, exon 3.	-2.1	0.001404191
RC_R09379_at	R09379	solute carrier family 11 (proton-coupled divalent metal ion transporters), member	-2.1	0.006004344
RC_R99092_at	R99092	EST, Moderately similar to (defline not available 5052951) [H.sapiens]	-2.1	0.016256526
X95325_s_at	X95325	cold shock domain protein A12p13.1	-2.1	0.025953179
RC_T56281_f_at	T56281	Human metallothionein (MT)I-F gene	-2.1	0.032089569
RC_R44397_at	R44397	ESTs	-2.1	0.000265391
RC_H27180_f_at	H27180	ESTs	-2.1	0.004317675
AA165312_at	AA165312	ESTs	-2.1	0.025559572
RC_AA279313_s_at	AA279313	methyl CpG binding protein 2Xq28	-2.1	0.030594523
HG4322-HT4592_at	AF141349	Homo sapiens beta-tubulin mRNA, complete cds.	-2.1	0.017120749
RC_H81413_f_at	H81413	high-mobility group (nonhistone chromosomal) protein isoforms I and Y6p21	-2.1	0.009976588
RC_W94333_at	W94333	ESTs, Highly similar to (defline not available 5107163) [H.sapiens]	-2.1	0.000435688
RC_AA455070_at	AA455070	eukaryotic translation initiation factor 3, subunit 1 (alpha, 35kD)	-2.1	0.025226928
RC_R11526_f_at	R11526	parathymosin17q12-q22	-2.1	0.027182202
RC_T15409_f_at	T15409	EST	-2.1	0.001478856
RC_H05625_f_at	H05625	ESTs	-2.1	0.024564209
RC_AA620461_at	AA620461	ESTs	-2.0	0.022844667
RC_AA449791_f_at	AA449791	EST	-2.0	0.025394324
RC_AA435769_s_at	AA435769	ESTs	-2.0	0.008375153
RC_N55502_at	N55502	ESTs	-2.0	0.021894439
AF001294_at	AF001294	tumor suppressing subtransferable candidate 311p15.5	-2.0	0.03566128
RC_Z40898_at	Z40898	ESTs, Highly similar to (defline not available 4929639) [H.sapiens]	-2.0	0.002289892

Normal1-Normal2 vs BPH-With Symptoms Table **TABLE 1**

Affy element	Genbank ID	Genbank Name	Fold-change N1-N2 vs With	p-value N1-N2 vs With
RC_AA436861_at	AA436861	ESTs	-2.0	0.00187676
M63573_at	M63573	peptidylprolyl isomerase B (cyclophilin B)15	-2.0	0.044239663
RC_T25732_f_at	T25732	KIAA0252 protein	-2.0	0.041237995
RC_R01257_at	R01257	ESTs, Weakly similar to (defline not available 4456991) [H.sapiens]	-2.0	0.005735841
RC_H91703_i_at	H91703	cell division cycle 2717q12-17q23.2	-2.0	0.001412925
RC_N34817_at	N34817	ESTs	-2.0	0.040996591
RC_R60777_at	R60777	ESTs, Weakly similar to KIAA0374 [H.sapiens]	-2.0	0.000245565
RC_AA386264_at	AA386264	ESTs, Weakly similar to MICROTUBULE-ASSOCIATED PROTEIN 1B [M.musc	-2.0	0.000541139
RC_AA251769_at	AA251769	ESTs, Weakly similar to Containing ATP/GTP-binding site motif A(P-loop): Simil	-2.0	0.008985897
RC_R56602_at	R56602	Ig superfamily proteinXq12-q13.3	-2.0	0.024051216
RC_AA397919_at	AA397919	ESTs	-2.0	0.029784087
RC_W37778_f_at	W37778	ESTs, Weakly similar to envelope protein [H.sapiens]	-2.0	0.043013942
AA248555_at	AA248555	ESTs	-2.0	0.000824698
RC_AA463693_at	AA463693	ESTs, Weakly similar to SERINE/THREONINE-PROTEIN KINASE NEK3 [H.sap	-2.0	0.002809026
W76181_at	W76181	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 2 (8kD, B8)5q31	-2.0	0.008370263
RC_AA171939_at	AA171939	ESTs	-2.0	0.015796116
U30999_at	U30999	U30999 Homo sapiens MV3 melanoma Homo sapiens cDNA clone memd	-2.0	0.007070546
RC_F03254_f_at	F03254	synuclein, alpha (non A4 component of amyloid precursor)4q21	-2.0	0.011479379
RC_H26288_at	H26288	ESTs, Weakly similar to !!!! ALU SUBFAMILY SC WARNING ENTRY !!!! [H.sapi	-2.0	0.000262324
RC_AA007158_f_at	AA007158	ESTs	-2.0	0.001870921
RC_Z38785_at	Z38785	Homo sapiens clone 23940 mRNA sequence	-2.0	0.013437083
RC_AA282247_at	AA282247	ESTs	-2.0	0.000515617
RC_T23935_s_at	T23935	ESTs, Weakly similar to protein-tyrosine phosphatase [H.sapiens]	-2.0	0.006493804
RC_R59593_at	R59593	ESTs	-2.0	0.014592934
RC_AA446241_at	AA446241	tropomyosin 2 (beta)9p13.2-p13.1	-2.0	0.040680667
RC_Z40556_at	Z40556	DJ222E13.1a.1 (C-terminal part of novel protein dJ222E13.1) (partial isoform 1)	-2.0	0.019444878
RC_AA159025_at	AA159025	ESTs, Highly similar to (defline not available 4680655) [H.sapiens]	-2.0	0.01375696
RC_H03387_s_at	H03387	estrogen-responsive B box protein17p11.2	-2.0	0.036382844
RC_H17333_at	H17333	EST	-2.0	0.018111182
RC_AA412722_s_at	AA412722	putative cyclin G1 interacting protein7	-2.0	0.006838915
U65579_at	U65579	NADH dehydrogenase (ubiquinone) Fe-S protein 8 (23kD) (NADH-coenzyme Q r	-2.0	0.013707565
RC_R88209_at	R88209	ESTs	-2.0	0.040272012
RC_Z38266_at	Z38266	Homo sapiens PAC clone DJ0777O23 from 7p14-p15	-2.0	0.009414008

Normal1-Normal2 vs BPH-Cancer Table **TABLE 2**

	Affy element	Genbank ID	Genbank Name	Fold-Change N1-N2 vs Cancer	p-value N1-N2 vs Cancer
upregulated	L49169_at	L49169	FBJ murine osteosarcoma viral oncogene homolog B19q13.3	18.8	0.03580379
	RC_N23730_s_at	N23730	v-fos FBJ murine osteosarcoma viral oncogene homolog14q24.3	16.5	8.9867E-05
	V01512_rna1_at	V01512_rna1	v-fos FBJ murine osteosarcoma viral oncogene homolog14q24.3	16.0	0.00121664
	RC_T90619_f_at	T90619	actin, gamma 117q25	15.7	0.04412419
	U20734_s_at	U20734	jun B proto-oncogene19p13.2	14.3	0.00440455
	U62015_at	U62015	insulin-like growth factor binding protein 101p22-p31	13.8	0.00048722
	AA374109_at	AA374109	ESTs, Moderately similar to (defline not available 5031506) [R.norvegicus]	13.0	0.02591146
	RC_T79768_at	T79768	ESTs	12.2	0.01894014
	RC_AA410383_at	AA410383	B-cell-homing chemokine (ligand for Burkitt's lymphoma receptor-1)4q21	11.1	0.04602578
	X52541_at	X52541	early growth response 15q31.1	9.7	0.00316754
	RC_N66802_at	N66802	early growth response 38p23-p21	9.7	0.02676479
	RC_AA463726_s_at	AA463726	JM27 proteinXp11.23	9.4	0.00340917
	N40141_at	N40141	JM27 proteinXp11.23	8.4	0.02176821
	M34996_s_at	M34996	major histocompatibility complex, class II, DQ alpha 16p21.3	7.7	0.01588621
	RC_T67053_f_at	T67053	immumoglobulin lambda gene cluster22q11.1-q11.2	7.4	0.00019687
	RC_AA404957_at	AA404957	ESTs, Highly similar to MATRIX GLA-PROTEIN PRECURSOR [H.sapiens]	6.6	0.01145138
	RC_H64493_f_at	H64493	immunoglobulin gamma 3 (Gm marker)14q32.33	6.5	0.00271635
	RC_N47686_s_at	N47686	solute carrier family 14 (urea transporter), member 1 (Kidd blood group)18q11-q12	6.3	0.01556889
	RC_W44760_s_at	W44760	frizzled-related protein2qter	6.3	0.01689104
	L19871_at	L19871	activating transcription factor 3	6.2	0.00760329
	M92934_at	M92934	connective tissue growth factor6q23.1	6.1	0.00104693
	M62831_at	M62831	immediate early protein19	5.8	0.00753286
	L22524_s_at	L22524	matrix metalloproteinase 7 (matrilysin, uterine)11q21-q22	5.8	0.0482898
	J03507_at	J03507	complement component 75p13	5.6	0.00240657
	RC_AA236455_r_at	AA236455	ESTs	5.5	0.02265354
	RC_AA450127_at	AA450127	growth arrest and DNA-damage-inducible, beta19p13.3	5.5	0.02322759
	RC_AA281345_f_at	AA281345	immediate early protein19	5.4	0.00366107
	RC_N30198_at	N30198	ESTs	5.3	0.00565776
	AFFX-HSAC07/X00351_5	X00351	Human mRNA for beta-actin	5.3	0.01547291
	D83018_at	D83018	nel (chicken)-like 212q13.11-q13.12	5.1	0.00377476
	J04111_at	J04111	Jun activation domain binding protein1p32-p31	5.0	0.00024307

Normal1-Normal2 vs BPH-Cancer Table **TABLE 2**

Affy element	Genbank ID	Genbank Name	Fold-Change N1-N2 vs Cancer	p-value N1-N2 vs Cancer
X51345_at	X51345	jun B proto-oncogene19p13.2	5.0	0.01717342
RC_AA398903_at	AA398903	ESTs, Weakly similar to !!!! ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	4.9	0.01457782
RC_H17550_at	H17550	ESTs	4.7	0.01207939
S81914_at	S81914	immediate early response 36p21.3	4.5	0.00621865
RC_AA250958_f_at	AA250958	EST	4.4	1.8834E-05
RC_AA446651_at	AA446651	ESTs	4.4	0.0260228
HG1872-HT1907_at	M28590	Human (clone pcDG-79) MHC HLA-DG protein 41 mRNA, partial cds.	4.3	0.00883052
RC_AA490667_at	AA490667	ESTs	4.3	0.04886302
RC_N67041_at	N67041	ESTs	4.1	0.00933369
V00563_at	V00563	immunoglobulin mu14q32.33	4.1	0.00430194
X57809_s_at	X57809	immumoglobulin lambda gene cluster22q11.1-q11.2	4.1	0.02537166
R69417_at	R69417	ESTs	4.1	0.04637318
J00231_f_at	J00231	immunoglobulin gamma 3 (Gm marker)14q32.33	4.0	0.00476602
RC_AA402903_f_at	AA402903	immunoglobulin gamma 3 (Gm marker)14q32.33	3.9	0.00017291
U21128_at	U21128	lumican12q21.3-q22	3.9	0.00070892
M12529_at	M12529	apolipoprotein E19q13.2	3.7	0.02685625
RC_AA436616_at	AA436616	ESTs	3.7	0.02086008
U72649_at	U72649	B-cell translocation gene 2 (pheochromacytoma cell-3)1q32	3.7	0.0024874
X03689_s_at	X03689	Human mRNA fragment for elongation factor TU (N-terminus)	3.7	0.04821902
AFFX-HSAC07/X00351_5	X00351	Human mRNA for beta-actin	3.6	0.02971727
RC_T62857_at	T62857	ESTs	3.6	0.00284654
Z74616_s_at	Z74616	collagen, type I, alpha 27q22.1	3.6	0.00432829
X06700_s_at	X06700	collagen, type III, alpha 1 (Ehlers-Danlos syndrome type IV, autosomal dominant)2q31	3.6	0.0105961
RC_H86112_f_at	H86112	KIAA0471 gene product1q24-q25	3.6	0.01701397
M57466_s_at	M57466	major histocompatibility complex, class II, DP beta 16p21.3	3.5	0.00592467
RC_F09281_at	F09281	ESTs	3.5	0.00684173
RC_R51831_at	R51831	ESTs	3.4	0.00094142
RC_H21814_f_at	H21814	immumoglobulin lambda gene cluster22q11.1-q11.2	3.4	0.0097671
RC_W86513_at	W86513	ESTs	3.4	0.00377648
RC_H40424_s_at	H40424	EST	3.4	0.01628391
X57025_at	X57025	insulin-like growth factor 1 (somatomedin C)12q22-q23	3.3	0.04048925

Normal1-Normal2 vs BPH-Cancer Table **TABLE 2**

Affy element	Genbank ID	Genbank Name	Fold-Change N1-N2 vs Cancer	p-value N1-N2 vs Cancer
RC_AA044219_at	AA044219	BK984G1.1 (PUTATIVE C-terminal end of a novel protein with Collagen triple helix repea	3.3	0.00176111
RC_AA028092_s_at	AA028092	transcription factor 216pter-qter	3.3	0.00340548
RC_AA446661_at	AA446661	ESTs	3.3	0.04118899
RC_D80063_f_at	D80063	ESTs	3.3	0.04958514
M92843_s_at	M92843	zinc finger protein homologous to Zfp-36 in mouse19q13.1	3.3	0.00617408
M34516_r_at	M34516	immunoglobulin lambda-like polypeptide 322q11.2	3.2	0.02344053
M87789_s_at	M87789	immunoglobulin gamma 3 (Gm marker)14q32.33	3.2	0.00453465
N75870_s_at	N75870	dual specificity phosphatase 15q34	3.2	0.00015743
RC_AA609309_at	AA609309	ESTs, Moderately similar to !!!! ALU SUBFAMILY SB2 WARNING ENTRY !!!! [H.sapiens	3.1	0.03780658
S59049_at	S59049	regulator of G-protein signalling 11q31	3.0	0.0024193
AFFX-HUMGAPDH/M331	M33197	Human GAPDH	3.0	0.03453829
RC_D51060_s_at	D51060	Jun activation domain binding protein1p32-p31	3.0	0.02239004
RC_T23468_at	T23468	ESTs	2.9	0.00163462
U30521_at	U30521	P311 protein	2.9	0.0094842
Z48501_s_at	Z48501	poly(A)-binding protein-like 13q22-q25	2.9	0.02639698
W73859_at	W73859	transcription factor 216pter-qter	2.9	0.03732618
AA093923_at	AA093923	tissue inhibitor of metalloproteinase 217q25	2.8	0.04156402
RC_AA236476_at	AA236476	ESTs, Weakly similar to (defline not available 4507549) [H.sapiens]	2.7	0.03830528
U10550_at	U10550	GTP-binding protein overexpressed in skeletal muscle8q13-q21	2.7	0.04065788
RC_N24902_at	N24902	E1B-55kDa-associated protein 5	2.7	0.03810507
RC_AA056121_at	AA056121	ESTs	2.7	0.0242857
RC_H98835_at	H98835	ESTs	2.7	0.01990144
K02405_f_at	K02405	Human MHC class II HLA-DQ-beta mRNA (DR7 DQw2), complete cds	2.7	0.00138806
U90552_s_at	U90552	butyrophilin, subfamily 3, member A16p23	2.7	3.9119E-05
RC_N59831_at	N59831	ESTs	2.7	0.04543669
L33799_at	L33799	procollagen C-endopeptidase enhancer7q22	2.7	0.01087928
RC_N59532_s_at	N59532	aminomethyltransferase (glycine cleavage system protein T)3p21.2-p21.1	2.6	0.02571229
D13628_at	D13628	angiopoietin 18q22.3-q23	2.6	0.02720484
AA156897_s_at	AA156897	Homo sapiens mRNA; cDNA DKFZp564I1922 (from clone DKFZp564I1922)	2.6	0.00158002
RC_N67876_s_at	N67876	insulin-like growth factor 1 (somatomedin C)12q22-q23	2.6	0.03992641
M73720_at	M73720	carboxypeptidase A3 (mast cell)3q21-q25	2.6	0 023299

Normal1-Normal2 vs BPH-Cancer Table **TABLE 2**

Affy element	Genbank ID	Genbank Name	Fold-Change N1-N2 vs Cancer	p-value N1-N2 vs Cancer
H49440_at	H49440	nudix (nucleoside diphosphate linked moiety X)-type motif 36p21.2	2.6	0.0024987
RC_AA250850_at	AA250850	adrenergic, beta, receptor kinase 222q11	2.5	0.04115609
RC_T49061_at	T49061	ESTs	2.5	0.00934004
W28214_at	W28214	ESTs	2.5	0.03767792
RC_H44631_s_at	H44631	immediate early protein19	2.5	0.0423037
D28137_at	D28137	bone marrow stromal cell antigen 219p13.2	2.5	0.02621233
RC_AA609027_at	AA609027	ESTs	2.5	0.03855062
RC_AA257093_r_at	AA257093	T-cell receptor, beta cluster7q35	2.4	0.00265323
RC_F13763_at	F13763	ESTs	2.4	0.01694928
RC_H08548_s_at	H08548	ATP citrate lyase17q12-q21	2.4	0.03699852
RC_AA436618_at	AA436618	ESTs	2.4	0.00178991
RC_W45664_s_at	W45664	5' nucleotidase (CD73)6q14-q21	2.4	0.00176273
AA082546_at	AA082546	ESTs	2.4	0.02179188
D10522_at	D10522	myristoylated alanine-rich protein kinase C substrate (MARCKS, 80K-L)6q22.2	2.4	0.01733369
RC_AA411860_at	AA411860	ESTs, Highly similar to (defline not available 4929723) [H.sapiens]	2.4	0.02766922
AB002340_at	AB002340	KIAA0342 gene product	2.3	0.0032387
U53445_at	U53445	downregulated in ovarian cancer 13	2.3	0.00936165
AA091278_at	AA091278	ESTs	2.3	0.04625369
RC_AA486072_i_at	AA486072	small inducible cytokine A5 (RANTES)17q11.2-q12	2.3	0.01281647
RC_T53590_s_at	T53590	cytochrome P450, subfamily XIA (cholesterol side chain cleavage)15q23-q24	2.3	4.2964E-05
RC_N91971_f_at	N91971	retinol-binding protein 1, cellular3q23	2.3	0.0251716
RC_AA043777_at	AA043777	ESTs	2.3	0.00449019
RC_H54764_at	H54764	EST, Weakly similar to X-linked retinopathy protein {C-terminal, clone XEH.8c} [H.sapien	2.3	0.03698043
RC_AA443923_at	AA443923	ESTs	2.3	0.02583324
U60975_at	U60975	Homo sapiens gp250 precursor, mRNA, complete cds.	2.3	0.0412382
M34516_at	M34516	immunoglobulin lambda-like polypeptide 322q11.2	2.3	0.04138864
RC_N36001_at	N36001	ESTs, Weakly similar to !!!! ALU CLASS C WARNING ENTRY !!!! [H.sapiens]	2.2	0.00044908
AF010193_at	AF010193	MAD (mothers against decapentaplegic, Drosophila) homolog 718	2.2	0.00539777
AFFX-HSAC07/X00351_5	X00351	Human mRNA for beta-actin	2.2	0.03785222
RC_AA158262_s_at	AA158262	calpastatin5q14-q22	2.2	0.00664896
RC_AA156565_at	AA156565	4-nitrophenylphosphatase domain and non-neuronal SNAP25-like 122q12	2.2	0.02090192

Normal1-Normal2 vs BPH-Cancer Table **TABLE 2**

Affy element	Genbank ID	Genbank Name	Fold-Change N1-N2 vs Cancer	p-value N1-N2 vs Cancer
Z11793_at	Z11793	selenoprotein P, plasma, 15q31	2.2	0.00118281
RC_D80059_s_at	D80059	ESTs	2.2	0.03353443
RC_AA450324_at	AA450324	ESTs	2.2	0.02483201
RC_N39415_at	N39415	osteoglycin (osteoinductive factor)	2.2	0.03200112
RC_T23622_at	T23622	ESTs	2.2	0.04041783
RC_AA599365_at	AA599365	decorin12q23	2.2	0.01132518
X62320_at	X62320	granulin17	2.2	0.04304386
RC_R85291_at	R85291	ESTs	2.2	0.00498769
M11313_s_at	M11313	alpha-2-macroglobulin12p13.3-p12.3	2.2	0.01154574
AA047151_at	AA047151	ESTs	2.2	0.03398758
RC_AA205724_at	AA205724	ESTs	2.2	0.00456937
RC_AA086264_i_at	AA086264	ESTs, Highly similar to (defline not available 4191348) [H.sapiens]	2.2	0.02063742
RC_R42424_at	R42424	ESTs	2.2	0.03360342
RC_AA347359_s_at	AA347359	lysozyme (renal amyloidosis)12	2.1	0.0287645
AA092716_at	AA092716	HLA-B associated transcript-36p21.3	2.1	0.03171735
RC_R42241_at	R42241	ESTs	2.1	0.00801397
RC_N57577_at	N57577	KIAA0663 gene product	2.1	0.03202888
RC_W67577_s_at	W67577	CD74 antigen (invariant polypeptide of major histocompatibility complex, class II antigen-	2.1	0.00207212
C02016_at	C02016	KIAA0447 gene product	2.1	0.00239989
RC_AA256268_at	AA256268	ESTs	2.1	0.0269568
RC_T96171_at	T96171	EST	2.1	0.01221923
X72841_at	X72841	retinoblastoma-binding protein 7	2.1	0.03377469
RC_R45698_at	R45698	ESTs	2.1	0.04997589
RC_N22006_s_at	N22006	EST	2.1	0.01113134
RC_N69222_at	N69222	ESTs	2.1	0.02225692
RC_H97538_at	H97538	ESTs	2.0	0.03795259
RC_AA039935_at	AA039935	dynein light chain, outer arm 422q12.3-q13.2	2.0	0.01148877
RC_AA084138_at	AA084138	ESTs	2.0	0.01112443
AB002379_at	AB002379	KIAA0381 protein	2.0	0.00053041
RC_AA460651_at	AA460651	heterogeneous nuclear protein similar to rat helix destabilizing protein10	2.0	0.02769789
RC_W02204_at	W02204	solute carrier family 24 (sodium/potassium/calcium exchanger), member 115q22	2.0	0.00115779

Normal1-Normal2 vs BPH-Cancer Table **TABLE 2**

	Affy element	Genbank ID	Genbank Name	Fold-Change N1-N2 vs Cancer	p-value N1-N2 vs Cancer
	Y08614_at	Y08614	exportin 1 (CRM1, yeast, homolog)2p16	2.0	0.03536837
	D31134_at	D31134	KIAA1075 protein	2.0	0.02119653
	M94880_f_at	M94880	major histocompatibility complex, class I, A6p21.3	2.0	0.02538217
	J03040_at	J03040	secreted protein, acidic, cysteine-rich (osteonectin)5q31.3-q32	2.0	0.03547255
	RC_N68350_at	N68350	ESTs	2.0	0.04291789
	RC_H48793_at	H48793	EST	2.0	0.00296551
	HG3543-HT3739_at	M29645	insulin-like growth factor 2 (somatomedin A)11p15.5	2.0	0.01971237
	RC_W33172_at	W33172	ESTs, Weakly similar to ORF2 [M.musculus]	2.0	0.00645411
	RC_R08850_at	R08850	ESTs	2.0	0.01136477
	W52638_at	W52638	ESTs	2.0	0.0106124
	M19045_f_at	M19045	lysozyme (renal amyloidosis)12	2.0	0.00456197
	RC_AA312946_s_at	AA312946	ESTs	2.0	0.0202722
	RC_AA235310_at	AA235310	ESTs	2.0	0.01195494
	X03100_cds2_at	X03100_cds2	Human mRNA for SB classII histocompatibility antigen alpha-chain	2.0	0.00240454
	RC_T16282_f_at	T16282	wee1+ (S. pombe) homolog11p15.3-p15.1	2.0	0.03147215
	RC_H66642_f_at	H66642	ESTs, Moderately similar to !!!! ALU SUBFAMILY SQ WARNING ENTRY !!!! [H.sapiens]	2.0	0.02460529
down-regulated	RC_AA342337_at	AA342337	ESTs, Moderately similar to !!!! ALU SUBFAMILY SQ WARNING ENTRY !!!! [H.sapiens]	-23.7	3.2634E-05
	RC_AA398908_at	AA398908	Human Chromosome 16 BAC clone CIT987SK-A-61E3	-21.7	0.04005363
	RC_H15143_s_at	H15143	Human clone 23575 mRNA, partial cds	-13.8	0.02826163
	RC_N80129_i_at	N80129	metallothionein 1L16q13	-12.6	0.00214604
	RC_AA465394_at	AA465394	ESTs	-12.6	0.00496116
	RC_AA236545_at	AA236545	ESTs	-12.5	0.03493817
	RC_W42778_at	W42778	Homo sapiens clone 24636 mRNA sequence	-12.3	0.01044942
	RC_T40895_at	T40895	ESTs	-12.0	0.01968535
	RC_H94475_s_at	H94475	alpha-2-plasmin inhibitor17pter-p12	-11.7	0.01291982
	RC_R71792_s_at	R71792	ESTs, Moderately similar to FAT-SPECIFIC PROTEIN FSP27 [M.musculus]	-10.4	0.00254036
	RC_AA609006_at	AA609006	ESTs	-7.5	0.01390298
	RC_AA026641_s_at	AA026641	secretory leukocyte protease inhibitor (antileukoproteinase)	-7.0	0.01850877
	X65614_at	X65614	S100 calcium-binding protein P4p16	-6.7	0.00563431
	X93036_at	X93036	phospholemman-like, expressed in breast tumors, 8kD	-6.6	0.00527827

Normal1-Normal2 vs BPH-Cancer Table **TABLE 2**

Affy element	Genbank ID	Genbank Name	Fold-Change N1-N2 vs Cancer	p-value N1-N2 vs Cancer
RC_T94447_s_at	T94447	ESTs, Moderately similar to (defline not available 4335935) [M.musculus]	-5.7	0.00689191
RC_AA405488_at	AA405488	ESTs	-5.5	0.00023986
RC_T73433_s_at	T73433	angiotensinogen1q41-qter	-5.5	0.0094182
M99487_at	M99487	folate hydrolase (prostate-specific membrane antigen) 111p11.2	-5.3	0.00806779
RC_W88568_at	W88568	glycogenin 2Xp22.3	-5.1	0.02473908
RC_AA460914_at	AA460914	ESTs	-5.0	0.02438555
X57129_at	X57129	H1 histone family, member 26p21.3	-4.8	0.0063225
RC_Z41642_at	Z41642	ESTs	-4.7	0.00952552
RC_R46074_at	R46074	transforming, acidic coiled-coil containing protein 210q26	-4.7	0.00132784
J03910_rna1_at	J03910_rna1	metallothionein 1G16q13	-4.6	0.00457428
RC_AA350265_at	AA350265	histone deacetylase A	-4.5	0.00289741
AA165312_at	AA165312	ESTs	-4.2	0.0054878
RC_AA419011_at	AA419011	Homo sapiens mRNA; cDNA DKFZp586D0823 (from clone DKFZp586D0823)	-4.0	0.01907956
RC_N92502_s_at	N92502	ESTs, Moderately similar to HERV-E integrase [H.sapiens]	-4.0	0.03014404
RC_F03969_at	F03969	ESTs, Weakly similar to tumorous imaginal discs protein Tid56 homolog [H.sapiens]	-4.0	0.01702461
X76717_at	X76717	metallothionein 1L16q13	-3.9	0.0011454
RC_AA416762_s_at	AA416762	nuclear receptor subfamily 1, group H, member 219q13.3-19q13.3	-3.8	0.0117353
RC_AA053424_at	AA053424	ESTs, Weakly similar to mucin Muc3 [R.norvegicus]	-3.8	0.00973743
X64177_f_at	X64177	metallothionein 1H16q13	-3.7	0.00329719
RC_N32748_at	N32748	ESTs	-3.6	0.02145417
RC_AA416685_at	AA416685	UNC13 (C. elegans)-like9p11-p12	-3.6	0.01633839
RC_AA505136_at	AA505136	ESTs	-3.5	0.0072004
RC_AA165313_at	AA165313	ESTs	-3.5	0.03764919
RC_F02245_at	F02245	monoamine oxidase AXp11.4-p11.3	-3.4	0.00548613
RC_AA004699_at	AA004699	putative translation initiation factor	-3.4	0.00057505
RC_AA599331_at	AA599331	ESTs	-3.4	0.01136457
RC_N26904_at	N26904	ESTs, Weakly similar to FK506/rapamycin-binding protein FKBP13 precursor [H.sapiens]	-3.3	0.04541061
RC_AA070752_s_at	AA070752	insulin receptor substrate 12q36	-3.3	0.02843376
RC_AA599522_f_at	AA599522	squamous cell carcinoma antigen recognised by T cells	-3.2	0.0053113
RC_N94303_at	N94303	ESTs	-3.1	0 00016072
RC_F10078_at	F10078	ESTs	-3.1	0.02246459

Normal1-Normal2 vs BPH-Cancer Table **TABLE 2**

Affy element	Genbank ID	Genbank Name	Fold-Change N1-N2 vs Cancer	p-value N1-N2 vs Cancer
RC_AA447537_at	AA447537	ESTs, Moderately similar to (defline not available 5360237) [M.musculus]	-3.1	0.00732373
L77701_at	L77701	human homolog of yeast mitochondrial copper recruitment gene	-3.0	0.00148993
RC_H27675_at	H27675	ESTs	-3.0	0.0161605
V00594_at	V00594	metallothionein 2A16q13	-2.9	0.00149526
U52969_at	U52969	Purkinje cell protein 421q22.2-q22.3	-2.9	6.3447E-05
RC_R42607_at	R42607	ESTs	-2.8	0.00896005
RC_AA451836_at	AA451836	ESTs	-2.7	0.00840159
RC_F04492_at	F04492	ESTs, Weakly similar to !!!! ALU SUBFAMILY J WARNING ENTRY !!!! [H.sapiens]	-2.7	0.00144305
RC_H77597_f_at	H77597	metallothionein 1H16q13	-2.7	0.00332868
RC_AA430388_at	AA430388	ESTs, Moderately similar to !!!! ALU SUBFAMILY SQ WARNING ENTRY !!!! [H.sapiens]	-2.7	0.000114
RC_T90190_s_at	T90190	H1 histone family, member 26p21.3	-2.7	0.03024271
RC_H16171_f_at	H16171	cleft lip and palate associated transmembrane protein 119q13.2-q13.3	-2.7	0.02341444
RC_AA022886_at	AA022886	ESTs, Weakly similar to phosphatidylinositol transfer protein [H.sapiens]	-2.7	0.00489294
RC_R28370_at	R28370	ESTs	-2.7	0.00372455
RC_AA261907_at	AA261907	ESTs, Weakly similar to (defline not available 3874144) [C.elegans]	-2.6	0.04368944
RC_W37778_f_at	W37778	ESTs, Weakly similar to envelope protein [H.sapiens]	-2.6	0.03075684
RC_T98019_at	T98019	EST, Highly similar to PEREGRIN [H.sapiens]	-2.5	0.03556668
RC_N33927_s_at	N33927	H2B histone family, member B6p21.3	-2.5	0.01309393
RC_R40431_at	R40431	Homo sapiens mRNA; cDNA DKFZp564D016 (from clone DKFZp564D016)	-2.5	0.00423554
RC_AA133756_at	AA133756	Rho-associated, coiled-coil containing protein kinase 22p24	-2.5	0.01238916
RC_AA152200_s_at	AA152200	ESTs	-2.5	0.00436614
W63793_at	W63793	S-adenosylmethionine decarboxylase 16q21-q22	-2.5	0.00571425
RC_AA410298_at	AA410298	ESTs	-2.5	0.01874462
X99728_at	X99728	H.sapiens NDUFV3 gene, exon 3	-2.5	0.00458038
RC_W78127_at	W78127	ESTs, Weakly similar to KIAA0425 [H.sapiens]	-2.5	0.00124016
RC_R96924_s_at	R96924	ESTs	-2.5	0.00651591
RC_H16768_at	H16768	ESTs	-2.5	0.00566924
X76180_at	X76180	sodium channel, nonvoltage-gated 1 alpha12p13	-2.5	0.00762502
RC_AA432162_at	AA432162	Homo sapiens mRNA; cDNA DKFZp586B2022 (from clone DKFZp586B2022)	-2.4	0.01019911
RC_H88798_at	H88798	ESTs	-2.4	0.00078314
RC_AA609312_at	AA609312	ESTs	-2.4	0.01624332

Normal1-Normal2 vs BPH-Cancer Table **TABLE 2**

Affy element	Genbank ID	Genbank Name	Fold-Change N1-N2 vs Cancer	p-value N1-N2 vs Cancer
RC_AA131919_at	AA131919	putative type II membrane protein	-2.4	0.00026479
RC_N80129_f_at	N80129	metallothionein 1L16q13	-2.4	0.00229702
RC_AA182030_at	AA182030	ESTs	-2.4	0.04163238
W70167_at	W70167	ESTs	-2.4	0.00395969
RC_AA599522_r_at	AA599522	squamous cell carcinoma antigen recognised by T cells	-2.4	0.00434708
RC_N52254_s_at	N52254	SH3-binding domain glutamic acid-rich protein21q22.3	-2.4	0.01117139
RC_N95495_at	N95495	small inducible cytokine A5 (RANTES)17q11.2-q12	-2.4	0.00243024
RC_T68873_f_at	T68873	metallothionein 1L16q13	-2.4	0.00320019
AA429539_f_at	AA429539	ESTs	-2.4	0.02075188
RC_AA435769_s_at	AA435769	ESTs	-2.4	0.00983235
RC_AA029356_at	AA029356	ESTs	-2.3	0.00720872
AA316686_s_at	AA316686	ESTs, Highly similar to huntingtin interacting protein HYPK [H.sapiens]	-2.3	0.00022575
RC_H02308_at	H02308	ESTs	-2.3	0.04177629
RC_AA258476_at	AA258476	Homo sapiens mRNA; cDNA DKFZp564J0323 (from clone DKFZp564J0323)	-2.3	0.02070961
X06956_at	X06956	tubulin, alpha 1 (testis specific)2q	-2.3	0.00365687
RC_H99694_at	H99694	ESTs	-2.3	0.01364534
RC_AA479044_s_at	AA479044	ESTs, Weakly similar to PROGASTRICSIN PRECURSOR [H.sapiens]	-2.3	0.0470323
RC_AA436861_at	AA436861	ESTs	-2.3	0.0017942
M24069_at	M24069	cold shock domain protein A12p13.1	-2.3	0.01412351
RC_AA410311_at	AA410311	ESTs	-2.3	0.04522701
W52858_at	W52858	Homo sapiens mRNA; cDNA DKFZp564F0522 (from clone DKFZp564F0522)	-2.3	0.0022764
RC_W38197_at	W38197	EST	-2.3	1.9602E-05
J00073_at	J00073	actin, alpha, cardiac muscle15q11-qter	-2.3	0.01847689
RC_D51069_f_at	D51069	melanoma adhesion molecule	-2.3	0.04269339
RC_AA504805_s_at	AA504805	interferon stimulated gene (20kD)15q26	-2.3	0.00880589
RC_F03254_f_at	F03254	synuclein, alpha (non A4 component of amyloid precursor)4q21	-2.3	0.00366891
M35252_at	M35252	transmembrane 4 superfamily member 3	-2.3	0.02808319
RC_AA040731_at	AA040731	ESTs	-2.2	0.02892481
RC_AA496247_at	AA496247	ESTs	-2.2	0.01333631
X59766_at	X59766	alpha-2-glycoprotein 1, zinc7	-2.2	0.00200351
RC_R84421_at	R84421	eukaryotic translation elongation factor 1 alpha 16q14	-2.2	0.01633371

Normal1-Normal2 vs BPH-Cancer Table **TABLE 2**

Affy element	Genbank ID	Genbank Name	Fold-Change N1-N2 vs Cancer	p-value N1-N2 vs Cancer
AA328993_s_at	AA328993	ESTs	-2.2	0.0044386
RC_R44535_f_at	R44535	endonuclease G9q34.1	-2.2	0.01431962
U41518_at	U41518	aquaporin 1 (channel-forming integral protein, 28kD)7p14	-2.2	0.00944746
RC_W33179_at	W33179	testis-specific kinase 21p32	-2.2	0.00110427
RC_H58873_s_at	H58873	solute carrier family 2 (facilitated glucose transporter), member 11p35-p31.3	-2.2	0.00023864
RC_R31679_s_at	R31679	ESTs	-2.2	0.01000414
RC_AA189083_at	AA189083	ESTs, Highly similar to (defline not available 4589468) [M.musculus]	-2.2	0.00246805
RC_AA251769_at	AA251769	ESTs, Weakly similar to Containing ATP/GTP-binding site motif A(P-loop): Similar to C.el	-2.2	0.01081902
RC_W70131_at	W70131	ESTs	-2.2	0.02955725
RC_R09379_at	R09379	solute carrier family 11 (proton-coupled divalent metal ion transporters), member 212q13	-2.2	0.00973051
RC_AA621695_at	AA621695	ESTs	-2.1	0.00199405
RC_H18947_at	H18947	ESTs	-2.1	0.02724627
RC_AA219552_s_at	AA219552	ESTs	-2.1	0.04651094
RC_N22620_at	N22620	ESTs	-2.1	0.01352739
RC_R02003_r_at	R02003	ESTs, Weakly similar to cappuccino [D.melanogaster]	-2.1	0.0105971
RC_AA405559_at	AA405559	ESTs	-2.1	0.0093056
RC_AA463693_at	AA463693	ESTs, Weakly similar to SERINE/THREONINE-PROTEIN KINASE NEK3 [H.sapiens]	-2.1	0.004157
RC_AA481407_at	AA481407	ESTs	-2.1	0.0027417
M11119_at	M11119	Human endogenous retrovirus envelope region mRNA (PL1)	-2.1	0.00371888
RC_AA159025_at	AA159025	ESTs, Highly similar to (defline not available 4680655) [H.sapiens]	-2.1	0.01112753
RC_AA411981_at	AA411981	ESTs, Weakly similar to putative seven pass transmembrane protein [H.sapiens]	-2.1	0.04429461
RC_W57931_at	W57931	ESTs, Moderately similar to CATHEPSIN D PRECURSOR [H.sapiens]	-2.1	0.00075574
X66899_at	X66899	Ewing sarcoma breakpoint region 122q12	-2.1	0.0020689
RC_R49327_at	R49327	solute carrier family 11 (proton-coupled divalent metal ion transporters), member 212q13	-2.1	0.03092884
RC_AA609645_at	AA609645	eukaryotic translation initiation factor 4 gamma, 13q27-qter	-2.1	0.04955957
RC_AA434108_at	AA434108	Homo sapiens heat shock protein hsp40-3 mRNA, complete cds	-2.1	0.03446875
X17567_s_at	X17567	small nuclear ribonucleoprotein polypeptides B and B120	-2.1	0.01447522
J04164_at	J04164	interferon-induced protein 17	-2.1	0.02341035
RC_AA135929_s_at	AA135929	ESTs, Highly similar to (defline not available 4103057) [M.musculus]	-2.1	0.00300907
L04270_at	L04270	lymphotoxin beta receptor (TNFR superfamily, member 312p13	-2.1	0.00677699
RC_H99035_at	H99035	ESTs	-2.1	0.00105388

Normal1-Normal2 vs BPH-Cancer Table **TABLE 2**

Affy element	Genbank ID	Genbank Name	Fold-Change N1-N2 vs Cancer	p-value N1-N2 vs Cancer
M64673_at	M64673	heat shock transcription factor 1	-2.1	0.004283
X85785_rna1_at	X85785_rna1	Duffy blood group1q21-q22	-2.1	0.00657464
M68864_at	M68864	Human ORF mRNA, complete cds	-2.1	0.01018583
D50928_at	D50928	KIAA0138 gene product	-2.1	0.00228306
RC_AA282247_at	AA282247	ESTs	-2.0	0.00797004
RC_R00144_at	R00144	ESTs	-2.0	0.00693985
RC_AA485965_at	AA485965	ESTs, Highly similar to (defline not available 4336766) [H.sapiens]	-2.0	0.00040504
S45630_at	S45630	crystallin, alpha B11q22.3-q23.1	-2.0	0.00615727
RC_T89703_at	T89703	ESTs, Highly similar to (defline not available 4455129) [H.sapiens]	-2.0	0.00028662
RC_Z38785_at	Z38785	Homo sapiens clone 23940 mRNA sequence	-2.0	0.00706437
X85373_at	X85373	small nuclear ribonucleoprotein polypeptide G	-2.0	6.9388E-05
RC_F04816_at	F04816	ESTs	-2.0	0.00535318
RC_AA043349_at	AA043349	ESTs	-2.0	0.01749596
RC_H84761_s_at	H84761	glutathione peroxidase 13p21.3	-2.0	0.00011662
M34338_s_at	M34338	spermidine synthase1p36-p22	-2.0	0.00856614
L13698_at	L13698	growth arrest-specific 19q21.3-q22.1	-2.0	0.01650451
RC_N75960_at	N75960	ESTs	-2.0	0.02408243
D45370_at	D45370	adipose specific 210	-2.0	0.03436216
RC_AA401965_at	AA401965	tumor suppressor deleted in oral cancer-related 111q13	-2.0	0.01119009
RC_F09315_at	F09315	discs, large (Drosophila) homolog 510q23	-2.0	0.02075304
RC_AA025370_at	AA025370	KIAA0872 protein	-2.0	0.02656556
RC_H52835_at	H52835	phytanoyl-CoA hydroxylase (Refsum disease)10pter-p11.2	-2.0	0.01502125
RC_H99648_s_at	H99648	DNA segment, single copy probe LNS-CAI/LNS-CAII (deleted in polyposis5q22-q23	-2.0	0.01211585
RC_AA430074_at	AA430074	ESTs	-2.0	0.00235505
RC_AA598939_at	AA598939	ESTs	-2.0	0.01138387
AA455001_s_at	AA455001	ESTs	-2.0	0.0001762
RC_F09684_at	F09684	ESTs	-2.0	0.00274168
D42073_at	D42073	reticulocalbin 1, EF-hand calcium binding domain11p13	-2.0	0.01288169
RC_AA598695_at	AA598695	ESTs, Weakly similar to !!!! ALU SUBFAMILY SX WARNING ENTRY !!!! [H.sapiens]	-2.0	4.7727E-06
D23662_at	D23662	neural precursor cell expressed, developmentally down-regulated 8	-2.0	0.00315614
RC_AA431470_at	AA431470	protein kinase (cAMP-dependent, catalytic) inhibitor gamma20q	-2.0	0.03869298

Normal1-Normal2 vs BPH-Cancer Table **TABLE 2**

Affy element	Genbank ID	Genbank Name	Fold-Change N1-N2 vs Cancer	p-value N1-N2 vs Cancer
RC_AA399273_at	AA399273	ESTs	-2.0	0.02940312
RC_AA142858_at	AA142858	ESTs	-2.0	0.00197166
RC_Z40715_at	Z40715	Homo sapiens mRNA; cDNA DKFZp586C201 (from clone DKFZp586C201)	-2.0	0.01720634
RC_AA490341_s_at	AA490341	ESTs	-2.0	0.00457094
RC_N67815_f_at	N67815	ESTs, Weakly similar to (defline not available 4680655) [H.sapiens]	-2.0	0.00299669
RC_N53359_at	N53359	ESTs	-2.0	0.03491616

Normal vs. BPH W/Symptoms Table

TABLE 3

up-regulated	Affy element	GenBank ID	GenBank Name	Fold-change	t
1	N40141_at	N40141	JM27 protein	17.4	-7.64
2	rc_N23730_s_at	N23730	v-fos FBJ murine osteosarcoma viral oncogene homolog	10.8	-7.54
3	rc_AA463726_s_at	AA463726	JM27 protein	10 0	-6.56
4	rc_N23352_s_at	N23352	proenkephalin	10.0	-4.53
5	rc_H64493_f_at	H64493	immunoglobulin heavy constant gamma 3 (G3m marker)	9 1	-4.36
6	V01512_rna1_at	V01512	v-fos FBJ murine osteosarcoma viral oncogene homolog	9 1	-7.40
7	rc_H05704_r_at	H05704	HCR (a-helix coiled-coil rod homologue)	8.1	-2.79
8	L49169_at	L49169	FBJ murine osteosarcoma viral oncogene homolog B	8.0	-5 81
9	rc_AA410383_at	AA410383	B-cell-homing chemokine (ligand for Burkitt's lymphoma receptor-1)	7.5	-3.95
10	rc_AA131322_s_at	AA131322	tryptase; alpha,tryptase, beta (tryptase II)	7.2	-2 81
11	R56183_s_at	R56183	eukaryotic translation initiation factor 3, subunit 6 (48kD)	6 9	-2 77
12	rc_AA461300_at	AA461300	ESTs	6.9	-7.08
13	J00231_f_at	J00231	immunoglobulin heavy constant gamma 3 (G3m marker)	6.7	-4 62
14	rc_AA427622_s_at	AA427622	collagen, type XIII, alpha 1	6.6	-8.25
15	rc_T90889_at	T90889	ESTs	5 6	-3.72
16	rc_AA402903_f_at	AA402903	immunoglobulin heavy constant gamma 3 (G3m marker)	5 6	-3.61
17	rc_T23622_at	T23622	ESTs	5.5	-5.24
18	rc_T62857_at	T62857	ESTs	5 4	-7.85
19	rc_AA256268_at	AA256268	ESTs	5.3	-6.86
20	rc_R44714_s_at	R44714	ESTs	5 3	-4.83
21	rc_AA236476_at	AA236476	transmembrane protein TENB2,	5.1	-3.13
22	rc_AA028092_s_at	AA028092	transcription factor 21	5 1	-5.24
23	rc_T90619_f_at	T90619	actin, gamma 1	5 0	-2.19
24	J00123_at	J00123	proenkephalin	5 0	-3.98
25	X52541_at	X52541	early growth response 1	4.9	-5.78
26	rc_AA620825_at	AA620825	CGI-43 protein	4.9	-4.59
27	rc_AA424530_s_at	AA424530	ESTs	4.9	-5.42
28	rc_AA386386_s_at	AA386386	procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), beta polypeptide (protein disulfide isomerase; thyroid hormone binding protein p55)	4.9	-2.64
29	U62015_at	U62015	cysteine-rich, angiogenic inducer, 61	4.9	-6.24
30	rc_AA188981_at	AA188981	highly expressed in cancer, rich in leucine heptad repeats	4.9	-6.67
31	rc_H21814_f_at	H21814	immunoglobulin lambda locus	4.9	-2.67
32	M60314_at	M60314	bone morphogenetic protein 5	4.7	-10.82
33	rc_T67053_f_at	T67053	immunoglobulin lambda locus	4.7	-2.84
34	rc_N47686_s_at	N47686	solute carrier family 14 (urea transporter), member 1 (Kidd blood group)	4.7	-3.27
35	rc_AA436616_at	AA436616	ESTs	4.7	-6.34
36	rc_H60595_s_at	H60595	progesterone binding protein	4.7	-2.66
37	rc_H88338_at	H88338	ESTs	4 7	-7.93
38	M33653_at	M33653	collagen, type XIII, alpha 1	4 6	-8.95
39	rc_N30198_at	N30198	ESTs	4.5	-5.87
40	D83018_at	D83018	nel (chicken)-like 2	4 5	-9.79
41	rc_Z39904_at	Z39904	ESTs	4 5	-6.27
42	H61295_s_at	H61295	CD4 antigen (p55)	4 4	-4.49
43	rc_AA281345_f_at	AA281345	immediate early protein	4 3	-6.62
44	rc_T23490_s_at	T23490	hypothetical protein FLJ20185	4 2	-5.25
45	rc_AA279760_at	AA279760	DKFZP584M182 protein	4 2	-3.73
46	rc_R25410_at	R25410	ESTs	4 2	-4.69
47	rc_T03229_f_at	T03229	ESTs	4 2	-3.37
48	rc_R93908_at	R93908	ESTs	4 2	-3.39
49	AA374109_at	AA374109	spondin 2, extracellular matrix protein	4 2	-1 97
50	rc_R45654_at	R45654	collagen, type XIII, alpha 1	4 2	-5.69
51	rc_H86112_f_at	H86112	KIAA0471 gene product	4 1	-4.00

Normal vs. BPH W/Symptoms Table **TABLE 3**

up-regulated	Affy element	GenBank ID	GenBank Name	Fold-change	t
52	rc_AA257093_r_at	AA257093	T cell receptor beta locus	4.1	-7.77
53	rc_AA456147_at	AA456147	general transcription factor IIIA	4.1	-6.23
54	U21128_at	U21128	lumican	4.1	-6 15
55	rc_AA057195_at	AA057195	TNF? elastin microfibril interface located protein	4.1	-2.22
56	M63438_s_at	M63438	immunoglobulin kappa variable 1D-8	4 0	-2.53
57	M57466_s_at	M57466	major histocompatibility complex, class II, DP beta 1	4.0	-3.91
58	rc_AA443923_at	AA443923	cat eye syndrome critical region gene 1	4.0	-3.01
59	rc_N39415_at	N39415	DKFZP586P2421 protein	4.0	-5.70
60	rc_W67225_at	W67225	KIAA0592 protein	4.0	-3.35
61	M62831_at	M62831	immediate early protein	4 0	-6.39
62	rc_AA404957_at	AA404957	matrix Gla protein	4.0	-3.84
63	rc_F02992_at	F02992	ESTs	4.0	-3.65
64	U69263_at	U69263	matrilin 2	3.9	-4.84
65	rc_AA448625_at	AA448625	slit (Drosophila) homolog 3	3.9	-4.13
66	X57025_at	X57025	insulin-like growth factor 1 (somatomedin C)	3 9	-3.93
67	AA151544_at	AA151544	matrix metalloproteinase 23B	3 8	-5.54
68	rc_F13763_at	F13763	ESTs	3 8	-6.39
69	rc_AA436655_at	AA436655	hypothetical protein FLJ10781	3 8	-5 13
70	M87789_s_at	M87789	immunoglobulin heavy constant gamma 3 (G3m marker)	3.8	-3.93
71	L44416_at	L44416	DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 17 (72kD)	3 8	-1 75
72	U20350_at	U20350	chemokine (C-X3-C) receptor 1	3 8	-6.50
73	rc_AA449749_at	AA449749	ESTs	3 8	-4.52
74	rc_W73790_f_at	W73790	immunoglobulin lambda-like polypeptide 1	3 7	-2.95
75	rc_AA281145_at	AA281145	ESTs	3 7	-1.77
76	rc_f09748_s_at	f09748	ESTs	3 7	-4.12
77	rc_T64211_at	T64211	HNOEL-iso protein	3 7	-5.35
78	rc_N80152_at	N80152	RNA binding motif protein 6	3 7	-2.40
79	rc_AA436618_at	AA436618	microtubule-associated protein 2	3.7	-4.67
80	T85532_f_at	T85532	ESTs	3.7	-1.90
81	rc_AA398280_at	AA398280	ESTs	3 6	-3.11
82	rc_T23468_at	T23468	CGI-119 protein	3 6	-4.67
83	AA195678_at	AA195678	actin binding protein; macrophin (microfilament and actin filament cross-linker protein)	3 6	-3.48
84	AB002335_at	AB002335	KIAA0337 gene product	3 6	-4.21
85	rc_AA598982_s_at	AA598982	KIAA1114 protein,trophinin	3 6	-4.58
86	J03507_at	J03507	complement component 7	3.6	-6.21
87	J04130_s_at	J04130	small inducible cytokine A4 (homologous to mouse Mip-1b)	3 5	-4.76
88	AA495865_at	AA495865	ESTs	3 5	-3 65
89	HG3543-HT3739_at	HG3543-HT3739	insulin-like growth factor 2 (somatomedin A)	3 5	-4.69
90	rc_AA599662_s_at	AA599662	KIAA0534 protein	3 5	-4.32
91	rc_AA486072_i_at	AA486072	small inducible cytokine A5 (RANTES)	3 5	-3.88
92	rc_Z39983_s_at	Z39983	KIAA0561 protein	3 5	-5.56
93	rc_F02333_at	F02333	hypothetical protein FLJ20093	3 5	-2.23
94	rc_AA151210_at	AA151210	ESTs	3 5	-4.20
95	rc_N92239_at	N92239	Wnt inhibitory factor-1	3 5	-3.06
96	rc_AA173223_at	AA173223	ESTs	3 5	-5.22
97	rc_T86148_s_at	T86148	pituitary tumor-transforming 1 interacting protein	3 5	-2 15
98	AA214688_at	AA214688	eukaryotic translation initiation factor 4B	3 5	-3.13
99	rc_AA216589_at	AA216589	ESTs	3 5	-4.40
100	rc_AA446661_at	AA446661	hypothetical protein FLJ10970	3 4	-3 69
101	AA082548_at	AA082546	ESTs	3 4	-4.12
102	rc_W46395_at	W46395	chromobox homolog 6	3 4	-2.41

Normal vs. BPH W/Symptoms Table **TABLE 3**

up-regulated	Affy element	GenBank ID	GenBank Name	Fold-change	t
103	rc_AA401433_at	AA401433	ESTs	3.4	-3.17
104	D62965_at	D62965	ESTs	3.4	-2.07
105	rc_AA057829_s_at	AA057829	growth arrest-specific 6	3.4	-2 00
106	rc_AA009755_at	AA009755	ESTs	3 3	-4.77
107	AA247204_at	AA247204	DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 16	3 3	-2.85
108	D13628_at	D13628	angiopoietin 1	3.3	-4 86
109	rc_N59866_at	N59866	ESTs	3.3	-4.39
110	rc_AA406371_at	AA406371	ESTs	3.3	-4.98
111	rc_N67876_s_at	N67876	insulin-like growth factor 1 (somatomedin C)	3.3	-3.06
112	M84526_at	M84526	D component of complement (adipsin)	3.3	-3.06
113	rc_AA234095_at	AA234095	hypothetical protein FLJ20701	3.3	-3.78
114	rc_D60074_s_at	D60074	cadherin 10 (T2-cadherin)	3 3	-5.05
115	rc_T49602_s_at	T49602	ESTs	3.3	-3.36
116	rc_n22006_s_at	n22006	ESTs	3.3	-3.88
117	rc_F04112_f_at	F04112	ESTs	3 3	-3.26
118	rc_T64223_s_at	T64223	carboxypeptidase A3 (mast cell)	3 3	-2.97
119	U23946_at	U23946	RNA binding motif protein 5	3.2	-3.48
120	rc_AA358038_at	AA358038	SH3-binding domain glutamic acid-rich protein like	3.2	-3 21
121	rc_AA019433_at	AA019433	ESTs	3 2	-3.88
122	X03689_s_at	X03689	eukaryotic translation elongation factor 1 alpha 1	3.2	-1.91
123	rc_H17550_at	H17550	ESTs	3.2	-2 90
124	rc_AA047880_at	AA047880	prothymosin, alpha (gene sequence 28)	3 2	-5 88
125	rc_AA084138_at	AA084138	ESTs	3.2	-7.93
126	rc_AA599365_at	AA599365	decorin	3.2	-4.42
127	rc_N91971_f_at	N91971	retinol-binding protein 1, cellular	3.2	-4.13
128	rc_T62873_at	T62873	ESTs	3.2	-2.12
129	rc_N49899_at	N49899	ESTs	3 2	-3.73
130	AA298981_at	AA298981	fibulin 5	3 2	-6.06
131	rc_AA479286_at	AA479286	ESTs	3.2	-3.54
132	J04111_at	J04111	v-jun avian sarcoma virus 17 oncogene homolog	3.2	-5 47
133	rc_AA465491_at	AA465491	Mad4 homolog	3 2	-2.75
134	W28548_at	W28548	ESTs	3 2	-3 59
135	AA308998_at	AA308998	endothelial differentiation-related factor 1	3.2	-2.89
136	rc_AA488432_at	AA488432	phosphoserine phosphatase	3.2	-3.48
137	rc_AA598991_at	AA598991	amyloid beta (A4) precursor protein-binding, family A, member 2 (X11-like)	3 1	-4.51
138	AA463311_at	AA463311	hypothetical protein similar to mouse Fbw5	3 1	-2 57
139	rc_AA147224_at	AA147224	ESTs	3.1	-4.41
140	rc_AA609504_at	AA609504	fibronectin leucine rich transmembrane protein 2	3.1	-3.81
141	U20734_s_at	U20734	jun B proto-oncogene	3 1	-3.37
142	U06863_at	U06863	follistatin-like 1	3 1	-2.48
143	W51743_at	W51743	ESTs	3.1	-2.95
144	rc_AA465093_at	AA465093	TIA1 cytotoxic granule-associated RNA-binding protein	3.1	-5.34
145	rc_AA219100_at	AA219100	DKFZP586P2421 protein	3.1	-4.09
146	rc_R42424_at	R42424	ESTs	3 1	-3.82
147	rc_W73038_at	W73038	ESTs	3 1	-2.23
148	AA091278_at	AA091278	hypothetical protein FLJ10793	3 1	-2.75
149	rc_AA620289_at	AA620289	PRO0518 protein	3 1	-2.55
150	rc_AA149579_at	AA149579	prostate cancer associated protein 1	3.1	-2.66
151	M21121_at	M21121	small inducible cytokine A5 (RANTES)	3 1	-4.97
152	rc_AA427890_at	AA427890	ESTs	3 1	-4.32
153	M34516_r_at	M34516	immunoglobulin lambda-like polypeptide 1	3 1	-3.47

Normal vs. BPH W/Symptoms Table

TABLE 3

up-regulated	Affy element	GenBank ID	GenBank Name	Fold-change	t
154	rc_AA233347_at	AA233347	zinc finger protein 216	3.1	-2 43
155	rc_W74533_at	W74533	latrophilin	3.1	-3.51
156	rc_AA029597_at	AA029597	bone morphogenetic protein 7 (osteogenic protein 1)	3.1	-3 80
157	rc_N91887_s_at	N91887	thymosin, beta, identified in neuroblastoma cells	3.1	-4.47
158	rc_AA205724_at	AA205724	ESTs	3.0	-6 70
159	U30521_at	U30521	P311 protein	3.0	-6.06
160	X07109_at	X07109	protein kinase C, beta 1	3 0	-4 90
161	D82348_at	D82346	potassium voltage-gated channel, KQT-like subfamily, member 2	3.0	-3.49
162	rc_AA478962_at	AA478962	ESTs	3 0	-3.35
163	rc_AA151428_s_at	AA151428	matrix metalloproteinase 23A,matrix metalloproteinase 23B	3.0	-2.78
164	rc_AA130349_at	AA130349	ESTs	3 0	-2 01
165	M18737_ma1_at	M18737	granzyme A (granzyme 1, cytotoxic T-lymphocyte-associated serine esterase 3)	3.0	-5.90
166	rc_N91461_at	N91461	ESTs	3.0	-3.43
167	rc_AA045481_at	AA045481	ESTs	3.0	-3.70
168	U91903_at	U91903	frizzled-related protein	3.0	-4 73
169	U19495_s_at	U19495	stromal cell-derived factor 1	3 0	-4.38
170	M33493_s_at	M33493	tryptase, alpha,tryptase, beta (tryptase II)	3.0	-3.12
171	Y12711_at	Y12711	progesterone binding protein	3.0	-2.33
172	rc_N58172_at	N58172	ESTs	3.0	-2.53
173	M12529_at	M12529	apolipoprotein E	3.0	-1.92
174	rc_AA412505_at	AA412505	ESTs	3.0	-3.35
175	U45955_at	U45955	glycoprotein M6B	3.0	-4.09
176	rc_H56673_at	H56673	ESTs	3.0	-4.25
177	L33799_at	L33799	procollagen C-endopeptidase enhancer	3.0	-4.72
178	rc_Z40186_at	Z40186	ESTs	3.0	-2.22
179	AA094800_at	AA094800	eukaryotic translation initiation factor 3, subunit 7 (zeta, 66/67kD)	2 9	-2.56
180	D21063_at	D21063	minichromosome maintenance deficient (S. cerevisiae) 2 (mitotin)	2.9	-5.27
181	rc_AA412049_at	AA412049	ESTs	2.9	-2.63
182	rc_AA599661_at	AA599661	ESTs	2.9	-8.62
183	L02870_s_at	L02870	collagen, type VII, alpha 1 (epidermolysis bullosa, dystrophic, dominant and recessive)	2.9	-4.69
184	rc_AA232266_s_at	AA232266	ESTs	2.9	-3 22
185	L02321_at	L02321	glutathione S-transferase M5	2 9	-3.33
186	rc_AA428325_at	AA428325	SEC14 (S. cerevisiae)-like 2	2.9	-3.52
187	D82534_at	D82534	f-box and leucine-rich repeat protein 5	2.9	-2.20
188	rc_T32113_at	T32113	KIAA0657 protein	2.9	-2.47
189	rc_R10896_at	R10896	cytochrome c oxidase subunit VIIa polypeptide 2 like	2.9	-1.99
190	rc_AA019034_i_at	AA019034	ESTs	2 9	-4.40
191	D28423_at	D28423	ESTs	2 9	-2.31
192	rc_AA609943_at	AA609943	ESTs	2.9	-3.86
193	W69302_at	W69302	ESTs	2.9	-2 68
194	rc_H01824_f_at	H01824	GATA-binding protein 2	2.9	-3.82
195	rc_T67105_s_at	T67105	ESTs	2.9	-5 49
196	rc_AA426372_s_at	AA426372	H1 histone family, member X	2 9	-2 53
197	rc_T98288_f_at	T98288	ESTs	2.9	-2.66
198	rc_N63047_at	N63047	ESTs	2 9	-5.25
199	U57316_at	U57316	GCN5 (general control of amino-acid synthesis, yeast, homolog)-like 2	2 9	-3.59
200	rc_AA219304_s_at	AA219304	alpha-2-macroglobulin	2.9	-1 76

Normal vs. BPH W/Symptoms Table **TABLE 4**

down-regulated	Affy element	GenBank ID	GenBank Name	Fold-change	t
1	rc_T40895_at	T40895	protein tyrosine phosphatase type IVA, member 1	16.5	5.19
2	rc_N80129_i_at	N80129	metallothionein 1L	12.6	3.54
3	rc_AA460914_at	AA460914	ESTs	7 4	4.58
4	rc_AA234996_s_at	AA234996	cytochrome c oxidase subunit VIa polypeptide 2	7 2	4 10
5	X66141_at	X66141	myosin, light polypeptide 2, regulatory, cardiac, slow	6 6	3.80
6	AA234634_f_at	AA234634	CCAAT/enhancer binding protein (C/EBP), delta	6.2	4 35
7	rc_AA419011_at	AA419011	prostate androgen-regulated transcript 1	6.1	3.87
8	rc_N94303_at	N94303	ESTs	5.8	5.96
9	M20543_at	M20543	actin, alpha 1, skeletal muscle	5.5	3.20
10	rc_AA085943_s_at	AA085943	troponin T1, skeletal, slow	5.5	3.02
11	X06825_at	X06825	tropomyosin 2 (beta)	5.2	3 35
12	AB000584_at	AB000584	prostate differentiation factor	5.1	3.80
13	M19309_s_at	M19309	troponin T1, skeletal, slow	5.0	3.41
14	rc_AA040433_at	AA040433	DKFZP586N2124 protein	5 0	2 62
15	rc_N32748_at	N32748	ESTs	5.0	3.36
16	rc_AA227926_at	AA227926	ESTs	4.8	5 39
17	rc_AA457566_at	AA457566	ESTs	4.7	4.22
18	rc_AA026641_s_at	AA026641	secretory leukocyte protease inhibitor (antileukoproteinase)	4.6	2.09
19	rc_AA053424_at	AA053424	serine/threonine protein kinase MASK	4 5	4.16
20	V00594_at	V00594	metallothionein 2A	4.5	3.71
21	rc_R16983_at	R16983	ESTs	4 5	3 23
22	U75272_s_at	U75272	progastricsin (pepsinogen C)	4.4	4.57
23	rc_T94447_s_at	T94447	cortic al thymocyte receptor (X. laevis CTX) like	4.4	3.50
24	U08021_at	U08021	nicotinamide N-methyltransferase	4.4	2.41
25	J03910_ma1_at	J03910	metallothionein 1G	4.3	2.79
26	rc_AA236545_at	AA236545	ESTs	4 2	2.41
27	rc_AA211443_at	AA211443	ESTs	4.2	4.49
28	rc_AA398908_at	AA398908	ESTs	4.2	2.64
29	X57129_at	X57129	H1 histone family, member 2	4.2	3.88
30	M21665_s_at	M21665	myosin, heavy polypeptide 7, cardiac muscle, beta	4.1	3.61
31	X65614_at	X65614	S100 calcium-binding protein P	4.1	4.03
32	rc_AA197112_r_at	AA197112	putative nuclear protein	4 1	3.07
33	M99487_at	M99487	folate hydrolase (prostate-specific membrane antigen) 1	4.0	2.65
34	X04201_at	X04201	neurotrophic tyrosine kinase, receptor, type 1	3.9	2.87
35	X05451_s_at	X05451	ESTs	3.9	3.26
36	rc_AA435720_i_at	AA435720	tubulin, alpha 2	3.9	2.20
37	rc_N92502_s_at	N92502	ESTs	3 8	3.11
38	L77701_at	L77701	COX17 (yeast) homolog, cytochrome c oxidase assembly protein	3.8	3 97
39	HG2157-HT2227_at	HG2157-HT2227	ESTs	3.8	4.08
40	X76717_at	X76717	metallothionein 1L	3.8	5.82
41	HG1067-HT1067_r_at	HG1067-HT1067	ESTs	3.7	3.02
42	rc_AA599331_at	AA599331	CGI-119 protein, uncharacterized bone marrow protein BM039	3.6	4.90
43	M20642_s_at	M20642	ESTs	3 6	3.48
44	rc_AA055163_at	AA055163	calsequestrin 2, cardiac muscle	3 6	3.66
45	rc_AA127946_at	AA127946	DKFZP586B2022 protein	3.6	4 40
46	rc_AA022886_at	AA022886	retinal degeneration B beta	3.6	3 51
47	rc_AA342337_at	AA342337	ESTs	3.5	2.57
48	X02544_at	X02544	orosomucoid 1	3.5	1.92
49	rc_T73433_s_at	T73433	angiotensinogen	3 5	3.10
50	M21494_at	M21494	creatine kinase, muscle	3 4	2.46
51	rc_AA488072_s_at	AA488072	cardiac ankyrin repeat protein	3 4	2.78

TABLE 4

Normal vs. BPH W/Symptoms Table down-regulated

	Affy element	GenBank ID	GenBank Name	Fold-change	t
52	rc_AA293187_s_at	AA293187	B-cell CLL/lymphoma 3	3.4	1.62
53	rc_AA599522_r_at	AA599522	squamous cell carcinoma antigen recognised by T cells	3 4	3,03
54	rc_AA405488_at	AA405488	ESTs	3.4	2.57
55	rc_AA461453_at	AA461453	calcium binding protein Cab45 precursor,	3 4	3.10
56	rc_AA609006_at	AA609006	ESTs	3 4	2.30
57	rc_N24761_at	N24761	TU12B1-TY protein	3,4	3.89
58	rc_AA432162_at	AA432162	DKFZP586B2022 protein	3,4	2.78
59	X06256_at	X06256	integrin, alpha 5 (fibronectin receptor, alpha polypeptide)	3.4	4.51
60	rc_AA045825_at	AA045825	ESTs	3 3	3,90
61	rc_AA478778_at	AA478778	ESTs	3 3	4 37
62	rc_N80129_f_at	N80129	metallothionein 1L	3 2	3,60
63	rc_AA182030_at	AA182030	pyruvate dehydrogenase kinase, isoenzyme 4	3,2	3 72
64	rc_AA102489_at	AA102489	hypothetical protein FLJ10337	3,2	2,20
65	rc_R46074_at	R46074	transforming, acidic coiled-coil containing protein 2	3 2	3 38
66	rc_AA599522_f_at	AA599522	squamous cell carcinoma antigen recognised by T cells	3,2	2 36
67	rc_AA165313_at	AA165313	ESTs	3 2	2,76
68	rc_AA429636_at	AA429636	hexokinase 2	3 2	3 12
69	rc_R71792_s_at	R71792	thrombospondin 1	3,1	2,31
70	U05861_at	U05861	aldo-keto reductase family 1, member C1 (dihydrodiol dehydrogenase 1; 20-alpha (3-alpha)-hydroxysteroid dehydrogenase),aldo-keto reductase family 1, member C2 (dihydrodiol dehydrogenase 2; bile acid binding protein, 3-alpha hydroxysteroid dehydrogenase, type III)	3.1	2,62
71	rc_AA410311_at	AA410311	ESTs	3 1	3 52
72	rc_AA505136_at	AA505136	ESTs	3,1	3 00
73	rc_T68873_f_at	T68873	metallothionein 1L	3,0	3,18
74	X00371_ma1_at	X00371	myoglobin	3 0	2.18
75	rc_AA099820_at	AA099820	ESTs	3,0	3,08
76	rc_T90190_s_at	T90190	H1 histone family, member 2	3 0	3,48
77	rc_AA227936_f_at	AA227936	parathymosin	3,0	1 76
78	X90568_at	X90568	titin	3 0	2.83
79	rc_AA004699_at	AA004699	orphan G-protein coupled receptor	3,0	2,23
80	rc_F03969_at	F03969	ESTs	2,9	2 53
81	X93036_at	X93036	FXYD domain-containing ion transport regulator 3	2 9	2,91
82	rc_R91484_at	R91484	ESTs	2,9	6,43
83	rc_AA025370_at	AA025370	KIAA0872 protein	2,9	2 87
84	X51441_s_at	X51441	serum amyloid A1	2 9	1,78
85	X64177_f_at	X64177	metallothionein 1H	2,9	3,36
86	rc_AA255480_at	AA255480	ECSIT	2,9	2 38
87	rc_AA476944_at	AA476944	ESTs	2 8	4,26
88	U78294_at	U78294	arachidonate 15-lipoxygenase, second type	2,8	1 82
89	rc_AA045487_at	AA045487	ESTs	2.8	2 75
90	rc_N74291_at	N74291	ESTs	2.8	1,88
91	rc_N91973_at	N91973	hypothetical protein,three prime repair exonuclease 1	2.8	1 97
92	D81655_at	D81655	ESTs	2 8	1,89
93	U53225_at	U53225	sorting nexin 1	2,8	3,16
94	rc_H77597_f_at	H77597	metallothionein 1H	2,8	2 98
95	K02215_at	K02215	angiotensinogen	2.8	3 05
96	rc_AA464728_s_at	AA464728	ESTs	2,7	3,80
97	rc_W49708_at	W49708	ESTs	2,7	3 52
98	rc_AA453435_at	AA453435	ESTs	2,7	4.78
99	rc_D11824_at	D11824	ESTs	2,7	3 70
100	rc_T56281_f_at	T56281	RNA helicase-related protein	2 7	2 62
101	rc_AA182882_at	AA182882	titin-cap (telethonin)	2,7	1 85

Normal vs. BPH W/Symptoms Table

TABLE 4

down-regulated	Affy element	GenBank ID	GenBank Name	Fold-change	t
102	rc_AA447522_at	AA447522	ESTs	2.7	3.27
103	rc_N26904_at	N26904	FK506 binding protein precursor	2.7	3 21
104	rc_AA131919_at	AA131919	putative type II membrane protein	2.7	4.15
105	rc_R89840_at	R89840	ESTs	2.7	2.23
106	rc_W31470_at	W31470	thyroid hormone receptor-associated protein, 95-kD subunit	2.7	2.85
107	rc_W92207_at	W92207	ESTs	2.7	4 07
108	U96094_at	U96094	sarcolipin	2.7	2.23
109	rc_W70131_at	W70131	ESTs	2.7	3 64
110	rc_AA435720_f_at	AA435720	tubulin, alpha 2	2.7	1.98
111	rc_AA284879_at	AA284879	ESTs	2 7	1.74
112	rc_H22453_at	H22453	ESTs	2.7	4 20
113	D14826_s_at	D14826	cAMP responsive element modulator	2 6	4.13
114	rc_N93798_at	N93798	protein tyrosine phosphatase type IVA, member 3	2.6	3.12
115	U41804_at	U41804	putative T1/ST2 receptor binding protein	2.6	4 37
116	rc_W20486_f_at	W20486	chromosome 21 open reading frame 56	2.6	2.74
117	rc_AA055768_at	AA055768	CGI-119 protein	2.6	2.13
118	rc_AA447977_s_at	AA447977	ESTs	2.6	3.22
119	AA380393_at	AA380393	SEC7 homolog	2.6	2.29
120	rc_N29568_at	N29568	thyroid hormone receptor-associated protein, 150 kDa subunit	2.6	2 46
121	rc_AA426374_f_at	AA426374	tubulin, alpha 2	2.6	3.20
122	rc_H94471_at	H94471	occludin	2.6	2.19
123	rc_AA252219_at	AA252219	ESTs	2.6	3 83
124	rc_AA402000_at	AA402000	ESTs	2.6	2.29
125	rc_Z38744_at	Z38744	putative gene product	2.6	4 18
126	AA045870_at	AA045870	ESTs	2.6	2.26
127	rc_R38678_at	R38678	ESTs	2.6	4.16
128	R39467_f_at	R39467	NEU1 protein	2.6	2.79
129	AA455001_s_at	AA455001	CGI-43 protein	2.6	5.34
130	rc_AA292328_at	AA292328	activating transcription factor 5	2.6	2.88
131	X57348_s_at	X57348	stratifin	2.6	2 48
132	rc_T95005_s_at	T95005	ESTs	2.5	3.30
133	AA410355_at	AA410355	ribosomal protein S6 kinase, 70kD, polypeptide 2	2.5	2 31
134	AA036900_at	AA036900	ESTs	2.5	2.45
135	rc_F02204_at	F02204	BAI1-associated protein 2	2.5	2 26
136	U26173_s_at	U26173	nuclear factor, interleukin 3 regulated	2.5	3.91
137	rc_AA477767_at	AA477767	ESTs	2.5	3.17
138	rc_AA504805_s_at	AA504805	interferon stimulated gene (20kD)	2.5	3.79
139	rc_R33627_i_at	R33627	ESTs	2 5	1 99
140	rc_T40995_f_at	T40995	alcohol dehydrogenase 3 (class I), gamma polypeptide	2.5	2.15
141	rc_R00144_at	R00144	ESTs	2 5	2.69
142	U02020_at	U02020	pre-B-cell colony-enhancing factor	2.5	4.20
143	rc_AA287832_at	AA287832	ESTs	2.5	3 80
144	AA429539_f_at	AA429539	hypothetical protein	2 5	2.35
145	rc_H05084_at	H05084	GDP-mannose pyrophosphorylase B	2 5	2.23
146	rc_AA405616_at	AA405616	ESTs	2 5	3.33
147	AA455381_at	AA455381	aldehyde dehydrogenase 5 family, member A1 (succinate-semialdehyde dehydrogenase)	2.4	2 60
148	M13955_at	M13955	keratin 7	2.4	2 22
149	rc_AA180314_at	AA180314	ESTs	2.4	2 53
150	M37984_rna1_at	M37984	troponin C, slow	2.4	2 10
151	M61764_at	M61764	tubulin, gamma 1	2.4	3 48
152	rc_AA150920_at	AA150920	KIAA0539 gene product	2.4	4 11

Normal vs. BPH W/Symptoms Table

TABLE 4

down-regulated	Affy element	GenBank ID	GenBank Name	Fold-change	t
153	X65965_s_at	X65965	superoxide dismutase 2, mitochondrial	2.4	2.37
154	X93510_at	X93510	LIM domain protein	2.4	2.39
155	rc_N48056_s_at	N48056	folate hydrolase (prostate-specific membrane antigen) 1	2.4	1.80
156	rc_N26713_s_at	N26713	ESTs	2.4	3.87
157	rc_AA282247_at	AA282247	ESTs	2.4	3.17
158	rc_D80617_at	D80617	KIAA0596 protein	2.4	2.02
159	rc_F02245_at	F02245	monoamine oxidase A	2.4	2.79
160	rc_R58878_at	R58878	ESTs	2.4	2.80
161	rc_W45531_at	W45531	ESTs	2.4	4.17
162	L25270_at	L25270	SMC (mouse) homolog, X chromosome	2.4	3.26
163	rc_W88568_at	W88568	glycogenin 2	2.4	1.90
164	rc_AA070752_s_at	AA070752	insulin receptor substrate 1	2.4	2.87
165	U24169_at	U24169	JTV1 gene,hypothetical protein PRO0992	2.4	3.41
166	rc_T15423_s_at	T15423	2',3'-cyclic nucleotide 3' phosphodiesterase	2.4	1.71
167	X78706_at	X78706	carnitine acetyltransferase	2.4	3.51
168	rc_T10695_i_at	T10695	enigma (LIM domain protein)	2.4	1.52
169	rc_AA430388_at	AA430388	HSPC160 protein	2.4	5.04
170	M68519_ma1_at	M68519	surfactant, pulmonary-associated protein A1	2.4	3.89
171	rc_AA421562_at	AA421562	anterior gradient 2 (Xenepus laevis) homolog	2.4	1.80
172	rc_T97243_at	T97243	prenyl protein protease RCE1	2.4	2.46
173	rc_T15409_f_at	T15409	ESTs	2.3	3.76
174	rc_T62918_at	T62918	ESTs	2.3	2.59
175	rc_R15108_at	R15108	ESTs	2.3	2.74
176	AA454908_s_at	AA454908	KIAA0144 gene product	2.3	2.77
177	rc_N64683_at	N64883	CGI-119 protein	2.3	2.27
178	rc_H99035_at	H99035	ESTs	2.3	4.34
179	Y08374_ma1_at	Y08374	chitinase 3-like 1 (cartilage glycoprotein-39)	2.3	2.94
180	rc_AA236241_at	AA236241	ESTs	2.3	1.57
181	U52969_at	U52969	Purkinje cell protein 4	2.3	3.49
182	rc_R11526_f_at	R11526	parathymosin	2.3	1.71
183	rc_T15850_f_at	T15850	ESTs	2.3	2.42
184	HG2259-HT2348_s_at	HG2259-HT2348	tubulin, alpha 1 (testis specific),tubulin, alpha, ubiquitous	2.3	2.91
185	rc_H15143_s_at	H15143	ortholog of rat pippin	2.3	1.45
186	rc_AA101767_at	AA101767	ESTs	2.3	3.52
187	rc_AA193197_at	AA193197	sarcomeric muscle protein	2.3	1.98
188	U03688_at	U03688	cytochrome P450, subfamily I (dioxin-inducible), polypeptide 1 (glaucoma 3, primary infantile)	2.3	2.97
189	rc_R37774_at	R37774	cytochrome P450 retinoid metabolizing protein	2.3	4.11
190	rc_H81413_f_at	H81413	high-mobility group (nonhistone chromosomal) protein isoforms I and Y	2.3	3.12
191	X16354_at	X16354	carcinoembryonic antigen-related cell adhesion molecule 1 (biliary glycoprotein)	2.3	2.54
192	rc_AA457235_at	AA457235	ESTs	2.3	2.25
193	D13643_at	D13643	KIAA0018 gene product	2.3	1.78
194	rc_N30856_at	N30856	solute carrier family 19 (thiamine transporter), member 2	2.3	3.45
195	M26311_s_at	M26311	S100 calcium-binding protein A9 (calgranulin B)	2.3	2.37
198	rc_Z40556_at	Z40556	CGI-96 protein	2.3	2.39
197	rc_N79070_at	N79070	ESTs	2.3	1.43
198	Z69881_at	Z69881	ATPase, Ca++ transporting, ubiquitous	2.3	3.87
199	rc_D60755_s_at	D60755	ESTs	2.3	2.30
200	rc_N94424_at	N94424	retinoic acid receptor responder (tazarotene induced) 1	2.2	1.09

Table 5

Up-regulated genes

Cluster	Fragment Name
1	rc_AA256268_at
1	rc_AA188981_at
1	rc_AA173223_at
1	rc_AA216589_at
1	rc_AA234095_at
1	rc_H17550_at
1	AA308998_at
1	rc_AA488432_at
1	rc_AA427890_at
1	rc_N91887_s_at
1	rc_AA045481_at
3	rc_T23622_at
3	rc_T23490_s_at
3	rc_AA620289_at
4	rc_H05704_r_at
4	rc_AA436616_at
4	rc_AA456147_at
4	rc_f09748_s_at, AA495865_at
4	rc_AA598982_s_at
4	HG3543-HT3739_at
4	rc_AA609504_at
5	rc_AA028092_s_at
5	U62015_at
5	rc_F13763_at
5	rc_AA205724_at
5	U30521_at
6	X52541_at
6	rc_AA281345_f_at, M62831_at
7	rc_n22006_s_at
7	rc_R42424_at

Down-regulated genes

Cluster	Fragment Name
1	rc_AA227926_at
1	rc_AA398908_at
1	L77701_at
1	rc_AA599331_at
1	AA455001_s_at
3	rc_AA022886_at
3	rc_N24761_at
3	X06256_at
4	HG1067-HT1067_r_at
4	rc_AA127946_at
4	rc_AA405488_at
5	AA234634_f_at
5	X65614_at
5	rc_T73433_s_at
5	rc_R91484_at
5	rc_N93798_at
6	rc_N94303_at
6	AB000584_at
6	rc_AA410311_at
6	rc_F02245_at
7	rc_T40895_at
7	rc_N80129_i_at, X76717_at, rc_N80129_f_at, rc_T68873_f_at
7	rc_N32748_at
7	V00594_at
7	J03910_rna1_at
7	X57129_at, rc_T90190_s_at
7	rc_AA182030_at
7	rc_AA505136_at
7	X64177_f_at, rc_H77597_f_at
7	rc_AA101767_at

Table 6. Number of representative genes expressed in prostatic tissues and cell lines

	Prostatic tissues	Cell Line			
		BRF-55T	PZ-HPV7	BPH-1	LNCaP
Up-regulated genes	61	33	22	20	20
Down-regulated genes	43	31	28	30	33
Total	104	64	50	50	53